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TRANSACTIONS

OF THE

COLLEGE OF PHYSICIANS

OF

PHILADELPHIA

THIRD SERIES

VOLUME THE THIRTY-FIRST

PHILADELPHIA
PRINTED FOR THE COLLEGE
1909

NOTICE.

The present volume of TRANSACTIONS contains the papers read before the College from January, 1909, to December, 1909, inclusive.

The Committee of Publication thinks it proper to say that the College holds itself in no way responsible for the statements, reasonings, or opinions set forth in the various papers published in its TRANSACTIONS.

EDITED BY

WILLIAM ZENTMAYER.

DORNAN, PRINTER.

COLLEGE OF PHYSICIANS OF PHILADELPHIA.

1909.

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LIST

OF THE

PRESIDENTS OF THE COLLEGE FROM THE TIME OF ITS INSTITUTION.

ELECTED	
1787	JOHN REDMAN
1805	WILLIAM SHIPPEN
1809	ADAM KUHN
1818	THOMAS PARKE
1835	THOMAS C. JAMES*
1835	THOMAS T. HEWSON
1848	GEORGE B. WOOD
1879	W. S. W. RUSCHENBERGER
1883	ALFRED STILLÉ
1884	SAMUEL LEWIS†
1884	J. M. DA COSTA
1886	S. WEIR MITCHELL
1889	D. HAYES AGNEW
1892	S. WEIR MITCHELL
1895	J. M. DA COSTA
1898	JOHN ASHHURST, JR.
1900	W. W. KEEN
1902	HORATIO C. WOOD
1904	ARTHUR V. MEIGS
1907	JAMES TYSON

* Died four months after his election.
† Resigned on account of ill-health.

FELLOWS

OF THE

COLLEGE OF PHYSICIANS OF PHILADELPHIA.

DECEMBER, 1909.

* Non-resident Fellows.
† Fellows who have commuted dues.

ELECTED

1892. Abbott, Alexander C., M.D., Sc.D. (Hon.), Professor of Hygiene and Bacteriology in the University of Pennsylvania; Member of the Board of Health of Philadelphia. 4229 Baltimore Ave.

1905. Adler, Lewis H., Jr., M.D., Professor of Diseases of the Rectum in the Philadelphia Polyclinic and College for Graduates in Medicine; Prosector to the Professor of Anatomy in the University of Pennsylvania; Consulting Surgeon to the Charity Hospital. 1610 Arch St.

1903. Allen, Alfred Reginald, M.D. Lecturer on Neurological Electro-Therapeutics and Instructor in Neurology and Neuropathology in the University of Pennsylvania. 111 S. Twenty-first St.

1906. Allen, Francis Olcott, Jr., A.B., M.D., Surgeon to the Dispensary of the Presbyterian Hospital; Surgeon to the Dispensary of the Methodist Episcopal Hospital. 323 S. Sixteenth St.

1896. Allyn, Herman B., M.D., Associate in Medicine in the University of Pennsylvania; Physician to the Philadelphia General Hospital. 501 S. Forty-second St.

1888. Anders, James M., M.D., LL.D., Professor of the Theory and Practice of Medicine and Clinical Medicine in the Medico-Chirurgical College; Consulting Physician to the Jewish Hospital Association, Philadelphia. 1605 Walnut St.

ELECTED

1869. Andrews, T. Hollingsworth, M.D. 1329 Spruce St.

1905. Anspach, Brooke M., M.D., Associate in Gynecology in the University of Pennsylvania; Assistant Gynecologist to the University Hospital; Gynecologist and Obstetrician to the Philadelphia General Hospital; Gynecologist to the Stetson Hospital. 119 S. Twentieth St.

1905. Appleman, Leighton F., M.D., Demonstrator of Pharmacy and Materia Medica, and Instructor in Therapeutics in the Jefferson Medical College; Instructor in Ophthalmology in the Philadelphia Polyclinic and College for Graduates in Medicine; Ophthalmologist to the Frederick Douglass Memorial Hospital. 308 S. Sixteenth St.

1906. Ashhurst, Astley P. C., A.B., M.D., Surgeon to the Dispensary of the Episcopal and of the Children's Hospitals; Assistant Surgeon to the Orthopaedic Hospital; Chief of the Gynecological Dispensary of the Pennsylvania Hospital; Prosector to the Associate Professor of Applied Anatomy in the University of Pennsylvania. 2000 De Lancey Place.

1893. Ashton, Thomas G., M.D., Adjunct Professor of Medicine in the University of Pennsylvania; Physician to the Philadelphia General Hospital. 1814 S. Rittenhouse Square.

1857. Atlee, Walter Franklin, A.M., M.D., Corresponding Member of La Société des Sciences Médicales de Lyons; Consulting Surgeon to St. Luke's Hospital, Bethlehem; Visiting Physician to the Preston Retreat. 210 S. Thirteenth St.

1906. Babbitt, James A., A.B. (Yale), A.M. (Haverford), M.D., Physical Director and Associate Professor of Physiology at Haverford College; Instructor in Diseases of the Nose and Throat in the Philadelphia Polyclinic; Laryngologist to the Dispensary of the Children's Hospital; Laryngologist and Aurist to the Home for the Training in Speech of Deaf Children before they are of School Age. 121 S. Eighteenth St.

1852. Bache, Thomas Hewson, M.D. 233 S. Thirteenth St.

1903. Bacon, John, M.D. Torresdale, Pa.

†1892. Baker, George Fales, B.S., M.D. 1818 Spruce St.

1889. Baldy, John Montgomery, M.D., Professor of Gynecology in the Philadelphia Polyclinic; Surgeon to the Gynecean Hospital; Consulting Surgeon to the Jewish and the Frederick Douglass Memorial Hospitals. 2219 De Lancey Place.

ELECTED

1898. Balliet, Tilghman M., A.M., M.D., Professor of Therapeutics at Dartmouth College, Hanover, N. H.; Physician to the Old Man's Home. 3709 Powelton Ave.

1883. Baum, Charles, A.M., M.D., Ph.D. 1828 Wallace St.

1908. Beardsley, Edward J. G., M.D., L.R.C.P. (Lond.), Demonstrator of Physical Diagnosis and Clinical Medicine in Jefferson Medical College; Clinical Pathologist and Physician to the Henry Phipps Institute; Assistant Physician to the Philadelphia General Hospital; Medical Superintendent of the Star Centre Charitable Association. 2030 Chestnut St.

1883. Beates, Henry, Jr., M.D., M.S. 260 S. Sixteenth St.

1874. Bennett, W. H., A.M., M.D., Physician-in-Charge of the Seashore House for Invalid Children, and of the Seaside House for Invalid Women, Atlantic City; formerly Physician to the Episcopal Hospital, and Physician-in-Charge of St. Christopher's Hospital for Children. 1837 Chestnut St.

1896. Beyea, Henry D., M.D., Associate in Gynecology and Assistant Demonstrator of Obstetrics in the University of Pennsylvania; Assistant Surgeon to the Gynecean Hospital. 1734 Spruce St.

†1884. Biddle, Alexander W., M.D. Chestnut Hill.

1884. Biddle, Thomas, M.D. 122 S. Twenty-second St.

*1903. Biggs, Montgomery H., M.D. Rutherfordton, N. C.

1908. Bland, P. Brooke, M.D., Instructor and Demonstrator of Gynecology in Jefferson Medical College; Assistant Gynecologist to the Jefferson Medical College Hospital; Assistant Gynecologist to St. Joseph's and the Philadelphia General Hospitals. 1729 Pine St.

1894. Bliss, Arthur Ames, M.D., Laryngologist and Aurist to the German Hospital; Consulting Laryngologist to the Pennsylvania Institution for the Deaf and Dumb. 117 S. Twentieth St.

1894. Bochroch, Max H., M.D., Demonstrator of Neurology and Chief Clinical Assistant in the Nervous Department of the Jefferson Medical College Hospital; Neurologist to the Out-patient Department of St. Joseph's Hospital. 937 N. Eighth St.

1896. Boger, John A., A.M., M.D., Surgeon to St. Mary's Hospital; Surgeon to the Stetson Hospital; Surgeon to the Dispensary of the Episcopal Hospital. 2213 N. Broad St.

ELECTED

1891. Boyd, George M., M.D., Professor of Clinical Obstetrics in the Medico-Chirurgical College; Obstetrician to the Medico-Chirurgical Hospital; Physician to the Philadelphia Lying-in Charity; Obstetrician and Gynecologist to the Philadelphia General Hospital. 1909 Spruce St.

1907. Boyer, Henry Percival, M.D., Physician to the Stetson Hospital; Assistant Physician to the Orthopaedic Hospital and Infirmary for Nervous Diseases. 4602 Baltimore Ave.

†1884. Bradford, T. Hewson, M.D., Medical Director of the Philadelphia Life Insurance Company; Medical Director of the United Security Life Insurance and Trust Company; Attending Physician to St. Martin's College for Destitute Boys. 125 S. Eighteenth St.

1907. Bradley, William N., Ph.G., M.D., Assistant Physician to the Medical Dispensary of the Children's Hospital. 1532 S. Sixth St.

1903. Branson, Thomas F., M.D., Attending Physician to the Bryn Mawr Hospital. Rosemont, Pa.

1891. Brinton, Lewis, M.D. 1933 Spruce St.

1900. Brinton, Ward, A.M., M.D., Visiting Physician to the Tuberculosis Department of the Philadelphia General Hospital; Visiting Physician to the Hospital for Poor Consumptives, at White Haven, Pa.; Visiting Physician to the Henry Phipps Institute for the Prevention, Treatment, and Cure of Tuberculosis; Visiting Physician to the Philadelphia Jewish Sanatorium for Consumptives. 1423 Spruce St.

1907. Brooks, Macy, A.B. (Princeton), M.D., Assistant Genito-urinary Surgeon to the Philadelphia General Hospital. 1314 Spruce St.

1887. Brubaker, Albert P., A.M., M.D., Professor of Physiology and Medical Jurisprudence in the Jefferson Medical College; Professor of Physiology and Hygiene in the Drexel Institute of Science, Art, and Industry. 105 N. Thirty-fourth St.

1851. Bullock, William R., M.D. 6439 Green St., Germantown, Phila.

1906. Burns, Stillwell C., M.D., Lecturer on Surgery in the Medico-Chirurgical College; Assistant Surgeon to the Medico-Chirurgical Hospital. 1326 Spring Garden St.

1892. Burr, Charles W., M.D., Professor of Mental Diseases in the University of Pennsylvania; Neurologist to the Philadelphia General Hospital. 1327 Spruce St.

ELECTED

1906. Butler, Ralph, M.D., Chief of the Dispensary for Diseases of the Ear at the University Hospital; Chief of the Dispensary for Diseases of the Ear, Nose, and Throat at the German Hospital; Assistant Laryngologist to the Philadelphia General Hospital; Demonstrator of Otology in the Philadelphia Polyclinic. 1824 Chestnut St.

*1908. Cadbury, William W., A.M., M.D., University Medical School, Canton, China.

†1907. Cadwalader, Williams B., M.D., Pathologist and Clinical Assistant to the Orthopædic Hospital and Infirmary for Nervous Diseases; Assistant Instructor in Nervous Diseases in the Philadelphia Polyclinic. 1710 Locust St.

1905. Cameron, George A., M.D., Physician to the Germantown Hospital. S. E. cor. School House Lane and Greene St., Germantown.

1905. Carmany, Harry S., M.D., Surgeon to St. Timothy's Hospital, Roxborough; Surgeon to the Dispensary of the Episcopal Hospital. 366 Green Lane, Roxborough.

1905. Carpenter, Herbert B., M.D., Physician to the Dispensary of the Children's Hospital. 1805 Spruce St.

1895. Carpenter, John T., M.D., Lecturer on Ophthalmology in the University of Pennsylvania; Assistant Ophthalmic Surgeon to the University Hospital; Attending Ophthalmologist to the Bryn Mawr Hospital. 1624 Walnut St.

1892. Cattell, Henry W., A.M., M.D., Editor of *International Clinics*, of *Lippincott's Medical Dictionary*, and of *Medical Notes and Queries;* Author of *Postmortem Pathology.* 3709 Spruce St.

1900. Chance, Burton, M.D., Assistant Surgeon to the Wills Eye Hospital; Ophthalmologist to the Germantown Dispensary and Hospital. 235 S. Thirteenth St.

1885. Chapin, John B., M.D., LL.D. (Jefferson and Williams), Physician-in-Chief to the Pennsylvania Hospital for the Insane. Pennsylvania Hospital for the Insane.

1900. Chase, Robert Howland, A.M., M.D., Superintendent of the Friends' Asylum for the Insane. Friends' Asylum, Frankford.

*1868. Cheston, D. Murray, M.D. Harwood P. O., Md.

1897. Cheston, Radcliffe, M.D., Visiting Physician to the Chestnut Hill Hospital; Consulting Physician to the Germantown

ELECTED

Hospital and to the Pennsylvania Institution for the Deaf and Dumb. Chestnut Hill.

1904. Christian, Hilary M., M.D., Clinical Professor of Genito-Urinary Diseases in the Medico-Chirurgical College; Professor of Genito-urinary Diseases in the Philadelphia Polyclinic. 1321 Spruce St.

1903. Chrystie, Walter, M.D. Bryn Mawr, Pa.

1899. Clark, John G., M.D., Professor of Gynecology in the University of Pennsylvania; Gynecologist-in-Chief to the University Hospital. 2017 Walnut St.

1897. Claxton, Charles, A.M., M.D. 5137 Morris St., Germantown.

1872. Cleemann, Richard A., M.D. 2135 Spruce St.

1896. Cleveland, Arthur H., M.D., Clinical Professor of Laryngology in the Medico-Chirurgical College; Laryngologist to the Medico-Chirurgical Hospital; Laryngologist and Aurist to the Presbyterian Hospital, and to the Pennsylvania Institution for the Deaf and Dumb. 256 S. Fifteenth St.

1903. Coates, George Morrison, A.B., M.D., Professor of Diseases of the Ear in the Philadelphia Polyclinic; Assistant Laryngologist to the Pennsylvania Hospital; Laryngologist to the Pennsylvania Institution for the Instruction of the Blind; Laryngologist to the Philadelphia Orphanage. 2032 Chestnut St.

1908. Codman, Charles A. E., M.D., Physician to the American Oncologic Hospital. 4116 Spruce St.

1907. Cohen, Myer Solis, A.B., M.D., Consulting Physician to the Hospital for Diseases of the Lungs, Chestnut Hill; Assistant Physician to the Philadelphia General Hospital; Pediatrician to the Dispensary of the Jewish Hospital; Visiting Physician to the Philadelphia Jewish Sanatorium for Consumptives. 4102 Girard Ave.

1888. Cohen, Solomon Solis, M.D., Professor of Clinical Medicine in the Jefferson Medical College; Physician to the Jefferson Medical College Hospital, to the Philadelphia General Hospital, to the Jewish Hospital, and to the Rush Hospital. 1525 Walnut St.

1898. Coles, Stricker, M.D., Assistant Professor of Obstetrics in the Jefferson Medical College; Assistant Obstetrician to the Jefferson and the Philadelphia General Hospitals. 2103 Walnut St.

1901. Coley, Thomas Luther, A.B., M.D., Attending Physician

ELECTED

to the Methodist Episcopal Hospital of Philadelphia. 338 S. Twenty-first St.

1903. Cooper, J. Cardeen, M.D., Consulting Physician to the Methodist Home for the Aged. 1016 Lehigh Ave.

1903. Coplin, W. M. L., M.D., Professor of Pathology in the Jefferson Medical College; Pathologist to and Director of the Laboratories of the Jefferson Medical College Hospital; Pathologist to the Philadelphia General Hospital and to the Friends' Asylum for the Insane, Frankford; Bacteriologist to the Pennsylvania State Board of Health. 606 South Forty-eighth St.

1907. Council, Malcolm S., M.D., Attending Physician to the Bryn Mawr Hospital; Attending Physician to the Cathcart Home at Devon. Bryn Mawr, Pa.

1909. Craig, Alexander R., A.M., M.D., Assistant Surgeon to the Methodist Hospital; Assistant Laryngologist to the Dispensary of the Children's Hospital.

1904. Craig, Frank A., M.D., Assistant Instructor in Medicine in the University of Pennsylvania; Member of Staff of the Henry Phipps Institute; Examining Physician to the Free Hospital for Poor Consumptives. 732 Pine St.

1907. Crampton, George S., M.D. 1700 Walnut St.

1895. Cross, William A., M.D., Consulting Physician to the Jewish Hospital. Jenkintown, Pa.

1904. Cruice, John M., M.D., Instructor in Medicine in the University of Pennsylvania; Assistant Physician to the Philadelphia General Hospital; Physician to the Medical Dispensary of the University Hospital and of St. Joseph's Hospital. 1815 Spruce St.

1902. Currie, Charles A., M.D., Physician to the Germantown Hospital. West Walnut Lane, Germantown.

1884. Curtin, Roland Gideon, A.M., M.D., Ph.D., Emeritus Physician to the Philadelphia General Hospital; Consulting Physician to the Presbyterian, St. Timothy's, and the Jewish Hospitals. 22 S. Eighteenth St.

1884. Da Costa, John C., M.D., Emeritus Gynecologist to the Jefferson Medical College Hospital; Consulting Gynecologist to St. Agnes' Hospital. 1022 Spruce St.

1903. Da Costa, John C., Jr., M.D., Demonstrator of Clinical Medicine in the Jefferson Medical College; Chief of the Medical Clinic in the Jefferson Medical College Hospital;

elected

Assistant Physician to the Philadelphia General Hospital; Hematologist to the German Hospital. 1022 Spruce St.

1896. Da Costa, John Chalmers, M.D., Professor of the Principles of Surgery and of Clinical Surgery in the Jefferson Medical College; Surgeon to the Philadelphia General and St. Joseph's Hospitals. 2045 Walnut St.

1887. Daland, Judson, M.D., Professor of Clinical Medicine in the Medico-Chirurgical College; Physician to the Medico-Chirurgical Hospital; Consulting Physician to the Kensington Hospital for Women; Consulting Physician to the State Hospital for the Insane at Norristown. 317 S. Eighteenth St.

1859. Darrach, James, M.D., Consulting Surgeon to the Germantown Hospital. 5923 Greene St., Germantown.

1896. Davis, Charles N., M.D., Dermatologist to the Pennsylvania Hospital; Consulting Dermatologist to St. Agnes' Hospital; Assistant Physician to the Dispensary for Skin Diseases in the Howard Hospital. 1931 Spruce St.

1888. Davis, Edward P., A.M., M.D., Professor of Obstetrics in the Jefferson Medical College and in the Philadelphia Polyclinic; Visiting Obstetrician to the Jefferson and the Polyclinic Hospitals; Obstetrician and Gynecologist to the Philadelphia General Hospital; Member of the American Gynecological Society, the American Pediatric Society, and of the International Congress of Obstetrics and Gynecology. 250 S. Twenty-first St.

1889. Davis, Gwilym G., M.D. (Univ. of Penna. and Göttingen), M.R.C.S. England, Associate Professor of Applied Anatomy in the University of Pennsylvania; Surgeon to the Episcopal, St. Joseph's, and the Orthopædic Hospitals. 1814 Spruce St.

1900. Davisson, Alex. Heron, M.D. 31 St. Paul's Road, Ardmore.

1894. Deaver, Harry C., M.D., Professor of Surgery in the Woman's Medical College of Pennsylvania; Surgeon to the Episcopal and the Stetson Hospitals, and to the Children's Hospital of the Mary J. Drexel Home. 1534 N. Fifteenth St.

1887. Deaver, John B., M.D., Surgeon-in-Chief to the German Hospital; Consulting Surgeon to the Germantown Hospital. 1634 Walnut St.

ELECTED

1892. Deaver, Richard Wilmot, M.D., Consulting Surgeon to the Germantown Hospital. 6105 Main St., Germantown.

1902. Dehoney, Howard, M.D. 237 S. Thirteenth St.

1885. Dercum, Francis X., M.D., Professor of Nervous and Mental Diseases in the Jefferson Medical College; Neurologist to the Philadelphia General Hospital; Consulting Neurologist to St. Agnes' and the Jewish Hospitals, and to the State Asylum for the Chronic Insane of Pennsylvania. 1719 Walnut St.

1908. Despard, Duncan L., M.D., Instructor in Surgery in Jefferson Medical College; Chief Assistant in the Surgical Clinic at Jefferson Medical College Hospital. 1806 Pine St.

1908. Dillard, Henry K., Jr., M.D., Physician to the Mary J. Drexel Home at the German Hospital. 234 S. Twentieth St.

1891. Dixon, Samuel G., M.D., Commissioner of Health of the Commonwealth of Pennsylvania; President of the Academy of Natural Sciences of Philadelphia; First Vice-President of the Zoölogical Society of Philadelphia; Member of the Board of Directors of the Wistar Institute of Anatomy of the University of Pennsylvania. Ardmore, Pa.

*1896. Donnellan, P. S., M.D., L.R.C.S. and P., Ireland. 151 E. Third St., Williamsport, Pa.

1897. Dorland, W. A. Newman, M.D., Associate in Gynecology in the Philadelphia Polyclinic and College for Graduates in Medicine; Assistant Instructor in Obstetrics in the University of Pennsylvania. 1623 Walnut St.

1907. Dorrance, George Morris, M.D., Assistant Surgeon to St. Agnes' Hospital; Assistant Oral Surgeon to the Philadelphia General Hospital; Instructor in Surgery in the Philadelphia Polyclinic; Demonstrator of Anatomy in the Dental Department of the University of Pennsylvania. 1716 Locust St.

1902. Dougherty, Sherborne W., M.D., Instructor in Physical Diagnosis in the University of Pennsylvania; Physician to the Dispensary of the German Hospital; Assistant Physician to the Methodist Hospital. 256 S. Sixteenth St.

1893. Downs, Norton, M.D. Fordhooke Farms, Three Tuns, Pa.

1864. Downs, R. N., M.D., Consulting Physician to the Germantown Hospital. 5916 Greene St., Germantown.

ELECTED

1902. Downs, Robert N., Jr., M.D., Surgeon to the Dispensary of the Germantown Hospital. 6008 Greene St., Germantown.

1864. Duer, Edward L., A.M., M.D., Gynecologist to the Presbyterian Hospital; Consulting Obstetrician to the Maternity Hospital and to the Preston Retreat. 1606 Locust St.

1897. Duer, S. Naudain, M.D., Physician to the Dispensary of the Presbyterian Hospital. 1916 Pine St.

1871. Duhring, L. A., M.D., Professor of Diseases of the Skin in the University of Pennsylvania; Honorary Member of the Dermatological Society of London, Società Itāliana di Dermatologia e Sifilographia, and Wiener Dermatologische Gesellschaft. 3322 Walnut St.

1881. Dulles, Charles Winslow, M.D., Consulting Surgeon of the Rush Hospital. 4101 Walnut St.

*1860. Dunton, William R., M.D. Montrose, Pa.

1899. Edsall, David L., M.D., Professor of Therapeutics and Pharmacology in the University of Pennsylvania; Physician to the Episcopal Hospital. 1432 Pine St.

*1887. Edwards, William A., M.D., Professor of Pediatrics in the Medical Department of the University of California. Fifth and Spring Sts., Los Angeles, Cal.

1904. Elmer, Walter G., M.D., Surgeon to the Out-patient Department of the Presbyterian Hospital; Instructor in Orthopedic Surgery in the University of Pennsylvania; Assistant Orthopedic Surgeon to the University Hospital; Consulting Physician to the Church Home for Children. 1801 Pine St.

1896. Ely, Thomas C., A.M., M.D. 2041 Green St.

1901. Erck, Theodore A., M.D., Assistant Surgeon to the Gynecean Hospital; Associate in Gynecology in the Philadelphia Polyclinic and College for Graduates in Medicine; Gynecologist to the Frederick Douglass Memorial Hospital. 251 S. Thirteenth St.

1893. Eshner, Augustus A., M.D., Professor of Clinical Medicine in the Philadelphia Polyclinic and College for Graduates in Medicine; Physician to the Philadelphia General Hospital; Assistant Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases; Physician to the Hospital for Diseases of the Lungs, Chestnut Hill. 1019 Spruce St.

1905. Evans, Joseph S., Jr., A.B., M.D., Instructor in Clinical Medicine in the University of Pennsylvania; Associate

ELECTED

in the William Pepper Laboratory of Clinical Medicine; Assistant Physician to the University Hospital. 2018 Locust St.

1905. Evans, William, M.D. 4007 Chestnut St.

1894. Faries, Randolph, M.D. 2007 Walnut St.

†1903. Farr, Clifford B., A.B., M.D., Professor of Diseases of the Stomach, etc., in the Philadelphia Polyclinic; Instructor in Medicine in the University of Pennsylvania; Assistant Physician to the Philadelphia General Hospital; Pathologist to the Presbyterian Hospital. 211 S. Seventeenth St.

1893. Farr, William W., M.D., Physician to the Leamy Home. 117 Allen's Lane, Mount Airy.

1884. Fenton, Thomas H., M.D., Ophthalmologist to St. Vincent's Home, to the Home for Aged Couples, to the Baptist Home, and to the House of the Good Shepherd. 1319 Spruce St.

1907. Ferguson, Albert D., M.D., Visiting Physician to the Widener Memorial School for Crippled Children. 1549 N. Thirteenth St.

1907. Fetterolf, George, A.B., M.D., Laryngologist to the Henry Phipps Institute for Tuberculosis; Laryngologist to the White Haven Sanatorium; Consulting Laryngologist to the Phœnixville Hospital; Demonstrator of Anatomy in the University of Pennsylvania. 330 S. Sixteenth St.

1907. Fife, Charles A., A.B., M.D., Instructor in Diseases of Children, and Associate in the William Pepper Clinical Laboratory in the University of Pennsylvania; Physician to St. Christopher's Hospital for Children, to the Children's Department of the Presbyterian Hospital, and to the Children's Department of the Mary J. Drexel Home; Assistant Pediatrist to the Philadelphia General Hospital; Visiting Physician to St. Vincent's Home. 2033 Locust St.

1884. Fisher, Henry M., M.D. 1027 Pine St.

1888. Flick, Lawrence F., M.D. 736 Pine St.

1908. Foulkrod, Collin, M.D., Assistant Obstetrician to the Presbyterian Hospital Maternity; Assistant Demonstrator of Obstetrics in Jefferson Medical College; Gynecologist to the Dispensary of the Presbyterian Hospital. 4022 Chestnut St.

1908. Fox, Herbert, M.D., Chief of the Laboratories of the

ELECTED

Pennsylvania Department of Health; Pathologist to the Laboratory of Comparative Pathology of the Zoölogical Society of Philadelphia; Pathologist to the Rush Hospital. 106 S. Thirty-eighth St.

†1885. Fox, Joseph M., M.D. Leesburg, Va.

1906. Fraley, Frederick, Jr., A.B., M.D. 314 S. Seventeenth St.

1903. Francine, Albert P., A.M., M.D., Instructor in Medicine in the University of Pennsylvania; Physician to the Medical Dispensary of the University Hospital; Attending Physician to the Philadelphia General Hospital, Department of Tuberculosis; Chief Physician to the State Dispensary for Tuberculosis, Philadelphia. 218 S. Fifteenth St.

1897. Frazier, Charles H., M.D., Professor of Clinical Surgery in the University of Pennsylvania; Surgeon to the University, the Philadelphia General, and the Episcopal Hospitals; Surgeon to the Home for Crippled Children. 1724 Spruce St.

†1890. Freeman, Walter J., M.D., Emeritus Professor of Laryngology in the Philadelphia Polyclinic; Laryngologist to the Orthopædic Hospital; Consulting Laryngologist to the Pennsylvania Institution for the Deaf and Dumb. 1832 Spruce St.

1893. Friebis, George, M.D., Ophthalmic Surgeon to the Lutheran Home and Orphanage, Mt. Airy. 1906 Chestnut St.

1889. Fussell, M. Howard, M.D., Assistant Professor of Medicine in the University of Pennsylvania; Physician to St. Timothy's Hospital; Physician to St. Mary's Hospital. 189 Green Lane, Manayunk.

1899. Gamble, Robert G., M.D., one of the Attending Physicians to the Bryn Mawr Hospital. Haverford, Pa.

1873. Gerhard, George S., M.D., Physician-in-Chief to the Bryn Mawr Hospital; Consulting Physician to Bryn Mawr College; Consulting Physician to Villa Nova College. Fifty-eighth Street and Overbrook Ave.

1902. Ghriskey, Albert A., M.D. 3936 Walnut St.

1892. Gibb, Joseph S., M.D., Professor of Diseases of the Throat and Nose in the Philadelphia Polyclinic; Surgeon to the Ear, Nose, and Throat Department of the Episcopal Hospital. 1907 Chestnut St.

1899. Gibbon, John H., M.D., Professor of Surgery in the Jefferson Medical College; Surgeon to the Pennsylvania and

ELECTED

the Bryn Mawr Hospitals; Consulting Surgeon to the Woman's Hospital. 1608 Spruce St.

1908. Gildersleeve, Nathaniel, M.D. Dormitories, University of Pennsylvania.

1897. Girvin, John H., M.D., Physician for Diseases of Women at the Presbyterian Hospital; Instructor in Obstetrics in the University of Pennsylvania. 3924 Walnut St.

1889. Githens, William H. H., M.D., Visiting Physician to the Sheltering Arms. 1337 Pine St.

1906. Gittings, J. Claxton, M.D., Visiting Physician to the Children's Hospital of the Mary J. Drexel Home, and to the Medical Dispensary of the Children's and the Presbyterian Hospitals; Assistant Pediatric Physician to the University Hospital; Instructor in Pediatrics in the University of Pennsylvania. 3942 Chestnut St.

1905. Given, Ellis E. W., M.D., Surgeon to the William L. Elkins Masonic Orphanage for Girls; Surgeon to the Dispensary of the Episcopal Hospital; Surgeon to the Dispensary of St. Christopher's Hospital for Children. 2714 Columbia Ave.

1894. Gleason, E. B., S.B., M.D., LL.D., Professor of Otology in the Medico-Chirurgical College. 2033 Chestnut St.

1906. Goepp, R. Max, M.D., Professor of Clinical Medicine and Dean of the Philadelphia Polyclinic and College for Graduates in Medicine. 332 S. Fifteenth St.

1906. Goldberg, Harold G., M.D., Curator and Pathologist to the Wills Eye Hospital; First Lieutenant and Assistant Surgeon to the Second Troop, Philadelphia City Cavalry, N. G. P. 1905 Chestnut St.

1893. Goodell, W. Constantine, M.D. 300 S. Thirteenth St.

1908. Goodman, Edward H., M.D., Assistant Instructor in Medicine in the University of Pennsylvania; Assistant Physician to the Medical Dispensary of the University Hospital; Dispensary Physician to the Presbyterian Hospital. 248 S. Twenty-first St.

1905. Gordon, Alfred, M.D., Associate in Nervous and Mental Diseases in the Jefferson Medical College; Neurologist to the Mt. Sinai, the Northwestern General, and the Douglass Memorial Hospitals. 1430 Pine St.

*†1897. Gould, George M., A.M., M.D. The Sentinels, Cayuga Heights, Ithaca, N. Y.

1894. Graham, Edwin E., M.D., Professor of Pediatrics in the

ELECTED

Jefferson Medical College; Pediatrist to the Jefferson and the Philadelphia General Hospitals; Physician to the Franklin Reformatory Home. 1713 Spruce St.

1885. Graham, John, M.D. 326 S. Fifteenth St.

1904. Grayson, Charles P., M.D., Clinical Professor of Laryngology and Rhinology in the University of Pennsylvania; Physician-in-Charge of the Throat and Nose Department of the University Hospital; Otolaryngologist to the Philadelphia General Hospital. 251 S. Sixteenth St.

1883. Griffith, J. P. Crozer, M.D., Clinical Professor of the Diseases of Children in the University of Pennsylvania; Physician to St. Agnes', the Children's, and the Methodist Hospitals. 1810 Spruce St.

1902. Gwyn, Norman B., M.D., Instructor in Medicine in the University of Pennsylvania. 23 S. Twenty-first St.

1894. Hamill, Samuel McC., M.D., Professor of Diseases of Children in the Philadelphia Polyclinic and College for Graduates in Medicine; Pediatrist to the Presbyterian Hospital; Pediatrist to St. Vincent's Home. 1822 Spruce St.

1897. Hand, Alfred, Jr., M.D., Visiting Physician to the Children's Hospital, to the Children's Hospital of the Mary J. Drexel Home, and to the Methodist Hospital. 1724 Pine St.

1886. Hansell, Howard F., M.D., Professor of Ophthalmology in the Jefferson Medical College; Ophthalmic Surgeon to the Philadelphia General Hospital and to the Jefferson Medical College Hospital; Emeritus Professor of Diseases of the Eye in the Philadelphia Polyclinic. 1528 Walnut St.

1889. Hare, Hobart A., M.D., Professor of Therapeutics in the Jefferson Medical College; Physician to the Jefferson Medical College Hospital. 1801 Spruce St.

1903. Hart, Charles D., M.A., M.D., Physician to the Outpatient Department of the Pennsylvania Hospital; Inspector of the Eastern Penitentiary. 1317 Walnut St.

1885. Harte, Richard H., M.D., Adjunct Professor of Surgery in the University of Pennsylvania; Surgeon to the Pennsylvania and to the Orthopædic Hospitals; Consulting Surgeon to St. Mary's, St. Timothy's, and the Bryn Mawr Hospitals. 1503 Spruce St.

1888. Hartzell, Milton B., M.D., Associate in Dermatology in the University of Pennsylvania; Clinical Professor of

ELECTED

Dermatology in the Woman's Medical College of Pennsylvania; Dermatologist to the Philadelphia General Hospital. 3644 Chestnut St.

1907. Hatfield, Charles James, A.B. (Princeton), M.D., Physician to the Henry Phipps Institute for the Study, Treatment, and Prevention of Tuberculosis; Visiting Physician to the White Haven Sanatorium. 2008 Walnut St.

1872. Hays, I. Minis, M.D. 266 S. Twenty-first St.

1882. Hearn, W. Joseph, M.D., Professor of Clinical Surgery in the Jefferson Medical College; Surgeon to the Philadelphia General Hospital. 1120 Walnut St.

1908. Heinleberg, Alfred, M.D., Demonstrator of Gynecology in the Jefferson Medical College; Assistant Gynecologist to St. Agnes' Hospital; Instructor in Therapeutics and Materia Medica in the Jefferson Medical College, and in the Philadelphia College of Pharmacy. 1327 Pine St.

1901. Heisler, John C., M.D., Professor of Anatomy in the Medico-Chirurgical College. 3829 Walnut St.

1884. Henry, Frederick P., M.D., Professor of the Principles and Practice of Medicine in the Woman's Medical College of Pennsylvania; Physician to the Philadelphia General Hospital; Corresponding Member of the Royal Academy of Medicine of Rome. 114 S. Eighteenth St.

1903. Henry, J. Norman, M.D., Clinical Professor of Medicine in the Woman's Medical College of Pennsylvania; Physician to the Pennsylvania Hospital; Assistant Physician to the Philadelphia General Hospital. 1624 Spruce St.

1891. Hewson, Addinell, A.M., M.D., Professor of Anatomy in the Philadelphia Polyclinic and College for Graduates in Medicine; Surgeon to St. Timothy's Hospital, Roxborough. 2120 Spruce St.

1909. Higbee, William S., M.D., President of the Pennsylvania State Board of Examiners for Registration of Nurses. 1703 S. Broad St.

1897. Hinkle, William M., M.D., Lecturer on the Anatomy and Physiology of the Vocal Organs in the National School of Elocution and Oratory. 1323 N. Thirteenth St.

*1892. Hinsdale, Guy, A.M., M.D., Secretary of the American Climatological Association; Corresponding Member of the Balneological and Climatological Section of the Royal Society of Medicine, England; Fellow of the American Academy of Medicine; Lecturer on Climatology in the

ELECTED

Medico-Chirurgical College, Philadelphia. Hot Springs, Virginia.

1888. Hirsh, A. Bern, M.D., Physician to the Home for Aged Couples. 1711 Diamond St.

1888. Hirst, Barton Cooke, M.D., Professor of Obstetrics in the University of Pennsylvania; Gynecologist to the Philadelphia General and the Howard Hospitals. 1821 Spruce Street.

1903. Hirst, John Cooke, M.D., Assistant Obstetrician to the University and the Philadelphia General Hospitals; Attending Physician to the Maternity Hospital and to the Gynecological Dispensary of the Howard Hospital; Consulting Obstetrician to the Southeastern Dispensary. 1618 Pine St.

1908. Hitchens, Arthur Parker, M.D., Special Lecturer in the Medico-Chirurgical College. Glenolden, Pa.

*1894. Hoch, William R., M.D. 1434 Glenarm St., Denver, Col.

1905. Hodge, Edward B., Jr., M.D., Surgeon to the Out-patient Department of the Pennsylvania Hospital; Assistant Surgeon to the Orthopædic Hospital; Dispensary Surgeon to the Presbyterian Hospital; Surgeon to the Children's Hospital. 346 S. Sixteenth St.

1885. Holland, James W., M.D., Professor of Medical Chemistry and Toxicology in the Jefferson Medical College. 2006 Chestnut St.

1906. Holloway, Thomas B., M.D., Instructor in Ophthalmology in the University of Pennsylvania; Assistant Ophthalmologist to the Orthopædic Hospital and Infirmary for Nervous Diseases; Ophthalmologist to the Pennsylvania Institution for the Instruction of the Blind; Consulting Ophthalmologist to the Maternity Hospital. 1819 Chestnut St.

1888. Horwitz, Orville, M.D., Professor of Genito-urinary Surgery in the Jefferson Medical College; Surgeon to the Jefferson Medical College Hospital, to St. Agnes' Hospital, and to the State Hospital for the Insane; Consulting Surgeon to the Jewish Hospital. 1721 Walnut St.

1908. Hoyt, Daniel M., M.D., Assistant Demonstrator of Pharmacology in the University of Pennsylvania; Physician to the Medical Dispensary of the University Hospital. 3604 Chestnut St.

1892. Hughes, William E., M.D., Visiting Physician to the Phila-

ELECTED

delphia General Hospital; Pathologist to the Presbyterian Hospital. 3945 Chestnut St.

1898. Hutchinson, James P., M.D., Surgeon to the Pennsylvania, the Methodist, the Children's, St. Timothy's, and the Bryn Mawr Hospitals; Adjunct Professor of Surgery in the University of Pennsylvania. 133 S. Twenty-second St.

1871. Ingham, James V., M.D. 1811 Walnut St.

*1885. Jackson, Edward, M.D., Professor of Ophthalmology in the University of Colorado; Emeritus Professor of Diseases of the Eye in the Philadelphia Polyclinic; Ophthalmologist to the Denver City and County Hospital. 1434 Glenarm St., Denver, Col.

1906. Jacobs, Francis Brinton, B.S., M.D., Pediatrist to the Howard Hospital; Pediatrist to the American Hospital for Diseases of the Stomach; Visiting Physician to the Philadelphia Orphan Asylum; Assistant in the Laboratory of the Polyclinic Hospital. 2032 Chestnut St.

1898. Johnson, Russell H., A.B. (Princeton), M.D., Physician to the Pennsylvania Institution for the Deaf and Dumb; Physician to the Chestnut Hill Hospital. Chestnut Hill, Philadelphia.

1900. Jones, Charles James, A.M., M.D., Ophthalmic Surgeon to the House of the Good Shepherd, Germantown; Assistant Surgeon to the Wills Eye Hospital. 1009 N. Sixth St.

1900. Jopson, John H., M.D., Surgeon to the Children's, the Presbyterian, and the Bryn Mawr Hospitals, and to the Philadelphia Home for Incurables. 1824 Pine St.

1900. Judson, Charles F., A.B., M.D., Physician to St. Christopher's Hospital for Children, to the Southern Home for Destitute Children, and to the Sheltering Arms. 1539 Pine St.

1902. Jump, Henry D., M.D., Instructor in Medicine in the University of Pennsylvania; Assistant Physician to the Medical Dispensary of the University Hospital. 4634 Chester Ave.

1886. Jurist, Louis, M.D. 916 N. Broad St.

1903. Kalteyer, Frederick J., M.D., Demonstrator of Clinical Medicine in the Jefferson Medical College; Chief of the Out-patient Department, Assistant Attending Physician

ELECTED

and Hematologist to the Jefferson Medical College Hospital; Pathologist to the Philadelphia Lying-in-Charity. 1533 Pine St.

1904. Kane, Bayard, M.D. 1632 Walnut St.

†1867. Keen, William W., M.D., LL.D. (Hon.), F.R.C.S. (Eng. and Edin.), Emeritus Professor of the Principles of Surgery and of Clinical Surgery in the Jefferson Medical College; Membre Correspondant Étranger de la Société de Chirurgie de Paris; Honorary Member of the Société Belge de Chirurgie and of the Clinical Society of London; Ehrenmitglied der deutschen Gesellschaft für Chirurgie. 1729 Chestnut St.

1897. Kelly, Aloysius O. J., A.M., M.D., Assistant Professor of Medicine in the University of Pennsylvania; Professor of the Theory and Practice of Medicine in the University of Vermont; Professor of Pathology in the Woman's Medical College of Pennsylvania; Physician to St. Agnes' Hospital, and Pathologist to the German Hospital. 1911 Pine St.

*1887. Kelly, Howard A., M.D., Professor of Gynecology in Johns Hopkins University and Gynecologist to the Johns Hopkins Hospital, Baltimore, Md. 1406 Eutaw Place, Baltimore, Md.

1909. Kelly, James A., A.M., M.D., Surgeon to St. Mary's Hospital; Pathologist and Instructor in Surgery in the Philadelphia Polyclinic and College for Graduates in Medicine. 1621 N. Seventeenth St.

1898. Kempton, Augustus F., M.D. 2118 Pine St.

1905. Kercher, Delno E., M.D. 1534 Pine St.

*1907. Kinyoun, Joseph J., M.D., Ph.D. (Georgetown), Professor of Pathology and Bacteriology in the George Washington University. 1423 Clifton St., Washington, D. C.

1895. Kneass, Samuel S., M.D., Associate in the William Pepper Laboratory of Clinical Medicine in the University of Pennsylvania. 1510 Walnut St.

1908. Knipe, Jay C., M.D., Ophthalmologist to the Jewish Hospital; Assistant Ophthalmologist to the Philadelphia General Hospital, and to the Mary J. Drexel Home; Chief of the Eye Clinic at the Jefferson Medical College Hospital; Demonstrator of Osteology and Syndesmology in the Jefferson Medical College. 2035 Chestnut St.

1808. Knowles, Frank Crozer, M.D., Assistant Dermatologist to the Philadelphia General Hospital; Dermatologist to

ELECTED

the Northern Dispensary, the Church Home for Children, and St. Vincent's Home; Assistant Dermatologist to the Hospital of the Woman's Medical College, and to the Dispensary of the Children's Hospital; Associate Dermatologist to the Dispensary of the Howard Hospital. 332 South Seventeenth St.

1904. Krauss, Frederick, M.D., Ophthalmic Surgeon to St. Christopher's Hospital for Children and Dispensary; Instructor in Ophthalmology in the Philadelphia Polyclinic. 1701 Chestnut St.

1905. Kremer, Walter H., M.D. 6122 Main St., Germantown.

1900. Krusen, Wilmer, M.D., Professor of Gynecology in the Medical Department of Temple University; Chief Gynecologist to the Samaritan and the Garretson Hospitals; Consulting Gynecologist to the Charity and Mercy Hospitals. 127 N. Twentieth St.

1897. Kyle, D. Braden, A.M., M.D., Professor of Laryngology in the Jefferson Medical College; Consulting Laryngologist, Rhinologist, and Otologist to St. Agnes' Hospital and to the Philadelphia Home for Incurables; Laryngologist to the New Jersey Training School for Feeble-minded Children; Bacteriologist to the Orthopædic Hospital and Infirmary for Nervous Diseases. 1517 Walnut St.

1909. Laird, J. Packard, M.D., Visiting Physician to the Devon Branch of the Presbyterian Hospital of Philadelphia. Devon, Pa.

1904. Landis, Henry R. M., M.D., Visiting Physician to the White Haven Sanatorium; Member of the Staff of the Henry Phipps Institute; Assistant Visiting Physician to the Philadelphia Hospital. 11 S. Twenty-first St.

1907. Langdon, H. Maxwell, M.D., Instructor in Ophthalmology in the University of Pennsylvania; Assistant Surgeon to the Dispensary for Diseases of the Eye in the University Hospital; Assistant Ophthalmologist to the Orthopædic Hospital; Ophthalmologist to the Methodist Episcopal Home for the Aged. 1728 Chestnut St.

1908. Lavenson, Ralph S., M.D., Assistant Physician to the Philadelphia General Hospital; Assistant Pathologist to the University Hospital; Associate in the William Pepper Laboratory of Clinical Medicine; Assistant Demonstrator of Gross Morbid Anatomy in the University of Pennsylvania. 1218 Locust St.

ELECTED

1904. Le Boutillier, Theodore, M.D., Clinical Professor of Pediatrics in the Woman's Medical College of Pennsylvania; Physician to the Dispensary of St. Christopher's Hospital for Children; Pediatrist to the Woman's College Hospital Dispensary; Visiting Physician to the Baptist Orphanage and to the Southern Home for Destitute Children. 216 S. Twentieth St.

1893. Le Conte, Robert G., A.B., M.D., Surgeon to the Pennsylvania and the Bryn Mawr Hospitals; Consulting Surgeon to the Germantown and the Gynecean Hospitals. 1530 Locust St.

1909. L'Engle, Edward M., M.D. Merion, Pa.

1887. Leaman, Henry, M.D. 832 N. Broad St.

1908. Lee, Walter E., M.D., Pennsylvania Hospital.

1903. Leffmann, Henry, A.M., M.D., D.D.S., Ph.D., Professor of Chemistry in the Woman's Medical College of Pennsylvania; Honorary Professor of Chemistry in the Wagner Free Institute of Science; Pathological Chemist to the Jefferson Medical College Hospital; Formerly Port Physician of Philadelphia. 1839 N. Seventeenth St.

1892. Leidy, Joseph, M.D., Officier l'instruction publique, France; Consulting Physician to the Pennsylvania Training School for Feeble-minded Children. 1319 Locust St.

1903. Leonard, Charles Lester, M.D. 112 S. Twentieth St.

1877. Lewis, Morris J., M.D., Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases and to the Pennsylvania Hospital. 1316 Locust St.

1904. Lindauer, Eugene, M.D., Instructor of Neurology in the Medico-Chirurgical Hospital; Associate in Clinical Medicine in the Philadelphia Polyclinic; Assistant Neurologist to the Philadelphia General Hospital. 2018 N. Thirty-second St.

1886. Lloyd, J. Hendrie, A.M. (Princeton), M.D., Neurologist to the Philadelphia General Hospital; Physician to the Methodist Episcopal Hospital, and to the Home for Crippled Children; Consulting Neurologist to the State Asylum for the Chronic Insane of Pennsylvania and to the Pennsylvania Training School for Feeble-minded Children. 3918 Walnut St.

1900. Lodge, John W., M.D., Consulting Physician to the Bryn Mawr Hospital. Merion, Pa.

1907. Lodholz, Edward, M.D., Demonstrator of Physiology in the University of Pennsylvania. 3103 Diamond St.

ELECTED

1893. Longaker, Daniel, M.D., Surgeon to the Jewish Maternity Hospital. 1402 N. Sixteenth St.

1906. Longcope, Warfield T., M.D., Director of the Ayer Clinical Laboratory of the Pennsylvania Hospital; Instructor in Medicine in the University of Pennsylvania. 342 S. Fifteenth St.

1877. Longstreth, Morris, M.D. 1416 Spruce St.

1907. Loux, Hiram R., M.D. 1614 N. Broad St.

1900. McCarthy, Daniel J., M.D., Professor of Medical Jurisprudence (George B. Wood Foundation) in the University of Pennsylvania; Neurologist to the Philadelphia General and St. Agnes' Hospitals, and to the Henry Phipps Institute. 1329 Spruce St.

1875. McClellan, George, M.D., Professor of Applied Anatomy in the Jefferson Medical College; Consulting Surgeon to the Howard Hospital. 1116 Spruce St.

*1903. McConnell, Guthrie, M.D., Bacteriologist to the Missouri State Board of Health; Pathologist to St. Luke's Hospital. 4175 Washington Ave., St. Louis, Mo.

1895. McFarland, Joseph, M.D., Professor of Pathology and Bacteriology in the Medico-Chirurgical College; Pathologist to the Medico-Chirurgical and to the Philadelphia General Hospital. 442 W. Stafford St., Germantown.

1905. McKenzie, Robert Tait, A.B., M.D., Professor of Physical Education and Director of the Department of Physical Education in the University of Pennsylvania. 26 S. Twenty-first St.

*1900. McReynolds, Robert Phillips, M.D. 213 S. Broadway, Los Angeles, Cal.

1886. MacCoy, Alexander W., M.D., Surgeon for Diseases of the Nose and Throat in the Out-patient Department of the Pennsylvania Hospital; Member of the American Laryngological Society. 216 S. Fifteenth St.

1901. MacLeod, George I., Jr., M.D., Physician to the Bryn Mawr Hospital; Assistant Physician to Bryn Mawr College. Ardmore, Pa.

1896. Makuen, G. Hudson, M.D., Professor of Defects of Speech in the Philadelphia Polyclinic; Laryngologist to St. Mary's Hospital and to the Frederick Douglass Memorial Hospital; Visiting Consultant on Defects of Speech to the New Jersey Training School for Feeble-minded Children. 1627 Walnut St.

ELECTED

1898. Marshall, George Morley, M.D., Laryngologist to the Philadelphia General Hospital; Physician and Laryngologist to St. Joseph's Hospital. 1819 Spruce St.

1893. Marshall, John, M.D., Nat.Sc.D., LL.D., Professor of Chemistry and Toxicology in the University of Pennsylvania. 1718 Pine St.

1889. Martin, Edward, M.D., Professor of Clinical Surgery in the University of Pennsylvania; Surgeon to the University, Howard, Philadelphia General, and Bryn Mawr Hospitals. 1506 Locust St.

1885. Mays, Thomas J., M.D., Visiting Physician to the Rush Hospital. 1829 Spruce St.

*1868. Mears, J. Ewing, A.B., A.M., M.D., LL.D. 1535 Land Title Building, Broad and Sansom Sts.

1875. Meigs, Arthur V., M.D., Physician to the Pennsylvania Hospital; Consulting Physician to the Pennsylvania Institution for the Instruction of the Blind. 1322 Walnut St.

*1894. Miller, D. J. Milton, M.D., Visiting Physician to the Children's Hospital. 1700 Pacific Ave., Atlantic City, N. J.

1881. Mills, Charles K., M.D., Professor of Neurology in the University of Pennsylvania; Neurologist to the Philadelphia General Hospital; Consultant to the Orthopædic Hospital and Infirmary for Nervous Diseases. 1909 Chestnut St.

1904. Mitchell, Charles F., M.D., Surgeon to the Germantown Hospital and to the Out-patient Department of the Pennsylvania Hospital; Assistant Surgeon to the Orthopædic Hospital and Infirmary for Nervous Diseases. 1503 Spruce St.

†1888. Mitchell, John K., M.D., Assistant Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases; Assistant Neurologist to the Presbyterian Hospital; Attending Physician to the Pennsylvania Training School for Feeble-minded Children. 1730 Spruce St.

1856. Mitchell, Silas Weir, M.A., M.D., LL.D. (Edinburgh, Harvard, Princeton, and Toronto), Corresponding Member of the French Academy of Medicine; Corresponding Member of the Verein für innerer Medicin, Berlin; Honorary Member of the Royal Medico-Chirurgical Society of London; Doctor of Medicine, Honoris Causa, University of Bologna. 1524 Walnut St.

ELECTED

1908. Montgomery, Charles M., A.B., M.D., Physician to the Henry Phipps Institute; Physician to the Home for Consumptives at Chestnut Hill; Physician to the Dispensary of the Episcopal Hospital; Examining Physician for the White Haven Sanatorium. 323 S. Sixteenth St.

1882. Montgomery, Edward E., M.D., Professor of Gynecology in the Jefferson Medical College; Gynecologist to the Jefferson Medical College Hospital and to St. Joseph's Hospital. 1703 Walnut St.

1886. Morris, Caspar, M.D. 2050 Locust St.

1893. Morris, Elliston J., M.D., Physician to the Episcopal Hospital and to the Midnight Mission. 128 S. Eighteenth St.

1883. Morris, Henry, M.D., Professor of Anatomy in the Woman's Medical College of Pennsylvania; Senior Visiting Physician to St. Joseph's Hospital; Associate Member, Military Surgeons of U. S. A. 313 S. Sixteenth St.

1856. Morris, J. Cheston, M.D. 1514 Spruce St.

1906. Morrison, William H., M.D. 8021 Frankford Ave.

1897. Morton, Samuel W., M.D. 1933 Chestnut St.

1891. Morton, Thomas S. K., M.D. School House Lane, Germantown.

1904. Moulton, Albert R., M.D., Senior Assistant Physician to the Pennsylvania Hospital for the Insane; Physician to the Out-patient Department for Nervous and Mental Diseases at the Pennsylvania Hospital; Professor of Mental Diseases in the Maine Medical School (Bowdoin College). Pennsylvania Hospital for the Insane.

1905. Müller, George P., M.D., Associate in Surgery in the University of Pennsylvania; Assistant Surgeon to the University and the Philadelphia General Hospitals; Surgeon to St. Christopher's Hospital for Children; Consulting Surgeon to the Chester County Hospital. 334 S. Fifteenth St.

1882. Musser, John H., M.D., Professor of Clinical Medicine in the University of Pennsylvania; Physician to the University, the Philadelphia General, and the Presbyterian Hospitals. 1927 Chestnut St.

1905. Mutschler, Louis H., M.D., Surgeon to the Dispensary of the Episcopal Hospital; Surgeon to the Dispensary of St. Christopher's Hospital for Children; Assistant Surgeon to the Orthopædic Hospital. 2030 Tioga St.

1896. Myers, T. D., M.D. 1521 Spruce St.

ELECTED

1902. Nassau, Charles F., M.D., Surgeon to St. Joseph's Hospital; Consulting Surgeon to the Frankford Hospital; Assistant Surgeon to the Jefferson Medical College Hospital; Associate in Surgery in the Jefferson Medical College. 1831 Chestnut St.

1886. Neff, Joseph S., M.D. 580 City Hall.

1887. Neilson, Thomas Rundle, A.M., M.D., Surgeon to the Episcopal Hospital and to St. Christopher's Hospital for Children; Clinical Professor of Genito-urinary Diseases in the University of Pennsylvania. 122 S. Seventeenth St.

1905. Newcomet, William S., M.D. 3501 Baring St.

1905. Newlin, Arthur, M.D., Physician to the Dispensary of the Children's Hospital; Assistant Physician to the Orthopædic Hospital. 253 S. Thirteenth St.

1899. Nicholson, William R., Jr., M.D., Assistant Instructor in Obstetrics in the University of Pennsylvania; Obstetrician to the Maternity Hospital; Assistant Surgeon to the Gynecean Hospital. 350 S. Fifteenth St.

1889. Noble, Charles P., M.D., Surgeon-in-Chief to the Kensington Hospital for Women; Surgeon-in-Charge of the Department for Women of the Northern Dispensary and of the Union Mission Hospital; Clinical Professor of Gynecology in the Woman's Medical College of Pennsylvania; Lecturer on Gynecology in the Philadelphia Polyclinic. 1509 Locust St.

1898. Nolan, Edward J., M.D., Recording Secretary and Librarian of the Academy of Natural Sciences of Philadelphia. 825 N. Twentieth St.

1905. Norris, Charles C., M.D., Instructor in Gynecology in the University of Pennsylvania; Obstetrician and Assistant Attending Physician to the Maternity Hospital; Gynecologist to the Philadelphia General Hospital. 1503 Locust St.

1905. Norris, George William, A.B., M.D., Associate in Medicine in the University of Pennsylvania; Assistant Physician to the Philadelphia General Hospital. 1530 Locust St.

*1901. Norris, Henry, M.D. Rutherfordton, N. C.

*1865. Norris, Isaac, M.D. Fairhill, Bryn Mawr, Pa.

1892. Norris, Richard C., M.D., Lecturer on Clinical and Operative Obstetrics in the University of Pennsylvania; Obstetrician in Charge of the Preston Retreat; Visiting Obstetrician to the Philadelphia General Hospital; Gynecologist to the

ELECTED

Methodist Episcopal Hospital, and Consulting Obstetrician and Attending Gynecologist to the Southeastern Dispensary and Hospital. 500 N. Twentieth St.

1884. Oliver, Charles A., A.M., M.D., Surgeon to the Wills Eye Hospital; Ophthalmic Surgeon to the Philadelphia General and the Presbyterian Hospitals; Consulting Ophthalmic Surgeon to St. Agnes' Hospital. 1507 Locust St.

*1884. O'Neill, J. Wilks, M.D. Bergenfield, N. J.

*1885. Osler, William, M.D., Regius Professor of Medicine in Oxford University, England. No. 7, Norman Gardens, Oxford, England.

1903. Ostheimer, Maurice, M.D., Senior Instructor in Pediatrics in the University of Pennsylvania; Physician-in-Charge of the Children's Dispensary, University Hospital; Physician to the Austro-Hungarian Consulate; Visiting Physician to the Baptist Orphanage. 118 S. Twenty-second St.

1897. Packard, Francis R., M.D., Surgeon to the Ear, Nose, and Throat Clinic of the Pennsylvania Hospital; Professor of Diseases of the Nose and Throat in the Philadelphia Polyclinic and College for Graduates in Medicine; Laryngologist to the Children's Hospital of Philadelphia; Consulting Aurist to the Bryn Mawr Hospital. 304 S. Nineteenth St.

1898. Page, Henry F., M.D., Assistant Physician to the German Hospital and Physician to the Medical Dispensary of the same; Instructor in Clinical Medicine in the Woman's Medical College of Pennsylvania; Physician to the Baptist Home. 1907 Girard Ave.

1906. Pancoast, Henry K., M.D., Lecturer on Skiagraphy in the University of Pennsylvania; Skiagrapher to the University Hospital. 4238 Pine St.

1909. Parish, Benjamin D., B.S., M.D., Assistant Instructor in Otology in the University of Pennsylvania; Assistant Surgeon to the Dispensary for Diseases of the Ear, University Hospital; Aurist and Laryngologist to St. Agnes' Hospital. 29 S. Nineteenth St.

1899. Parke, William E., M.D., Consulting Obstetrician to the Episcopal Hospital; Assistant Surgeon to the Kensington Hospital for Women; Associate Surgeon to the Department for Diseases of Women of the Northern Dispensary. 1739 N. Seventeenth St.

ELECTED

*1903. Pearce, Richard M., M.D., Professor of Pathology in the University and Bellevue Hospital Medical College. Carnegie Laboratory, 338 E. Twenty-sixth St., New York.

1909. Pemberton, Ralph, B.S., M.S., M.D., Woodward Fellow in Physiological Chemistry in the William Pepper Laboratory of Clinical Medicine in the University of Pennsylvania; Assistant Instructor in Medicine in the University of Pennsylvania; Physician to the Out-patient Department of the Presbyterian Hospital. 1947 Locust St.

†1889. Penrose, Charles Bingham, M.D., Ph.D. (Harvard), Formerly Professor of Gynecology in the University of Pennsylvania. 1720 Spruce St.

†1902. Pepper, William, M.D., Instructor in Medicine in the University of Pennsylvania. 1811 Spruce St.

1884. Perkins, Francis M., M.D., Ophthalmic Surgeon to St. Agnes' Hospital. 1428 Pine St.

1905. Pfahler, George E., M.D., Director of the Röntgen Ray Laboratory of the Medico-Chirurgical Hospital. 1321 Spruce St.

1907. Pfromm, George W., Ph.G., M.D. 1434 N. Fifteenth St.

1907. Phillips, Horace, M.D., Second Assistant Physician to the Pennsylvania Hospital for the Insane; Visiting Physician to the Eastern Penitentiary of Pennsylvania. Pennsylvania Hospital for the Insane.

1883. Piersol, George A., M.D., Professor of Anatomy in the University of Pennsylvania. 4722 Chester Ave.

1905. Pitfield, Robert L., M.D., Pathologist to the Germantown Hospital; Bacteriologist to the Chestnut Hill Hospital for Lung Diseases. 5211 Wayne Ave.

1896. Posey, William Campbell, M.D., Surgeon to the Wills Eye Hospital; Professor of Ophthalmology in the Philadelphia Polyclinic and College for Graduates in Medicine; Ophthalmic Surgeon to the Howard Hospital; Ophthalmologist to the Pennsylvania Hospital for Epileptics. 2049 Chestnut St.

1902. Potts, Barton H., M.D., Laryngologist and Aurist to the German and St. Mary's Hospitals; Assistant Aural Surgeon and Chief of the Ear Dispensary of the Children's Hospital; Laryngologist to the Pennsylvania Training School for Feeble-minded Children. 109 S. Twentieth St.

1899. Potts, Charles S., M.D., Professor of Neurology in the Medico-Chirurgical College; Neurologist to the Philadel-

ELECTED

phia General Hospital; Consultant to the Insane Department of the Philadelphia General Hospital; Consultant to the Hospital for the Insane, Atlantic County, New Jersey. 1728 Chestnut St.

1905. Prendergast, Michael T., M.D. 1735 Diamond St.

1907. Price, George E., M.D., Assistant Professor of Nervous and Mental Diseases in the Jefferson Medical College; Assistant Neurologist to the Philadelphia General Hospital. 1700 Walnut St.

†1889. Price, Joseph, M.D., Obstetric Physician to the Philadelphia Dispensary. 241 N. Eighteenth St.

1903. Purves, George Morehouse, M.D., Registrar of the Surgical Dispensary of the Hospital of the University of Pennsylvania. 4204 Walnut St.

†1903. Pyle, Walter L., A.M., M.D., Member of the American Ophthalmological Society; Assistant Surgeon to the Wills Eye Hospital. 1931 Chestnut St.

1908. Radcliffe, McCluney, A.M. (Lafayette), M.D., Attending Surgeon to the Wills Eye Hospital. 1812 Chestnut St.

1887. Randall, B. Alexander, M.A., M.D., Clinical Professor of Diseases of the Ear in the University of Pennsylvania; Ear Surgeon to the Children's Hospital; Consulting Aurist to the Pennsylvania Institution for the Deaf and Dumb, and to St. Timothy's Hospital. 1717 Locust St.

*1904 Ravenel, Mazyck P., M.D., Professor of Bacteriology in the University of Wisconsin. Madison, Wis.

1887. Reed, Charles H., M.D. 121 S. Seventeenth St.

1885. Reichert, Edward T., M.D., Professor of Physiology in the University of Pennsylvania. University of Pennsylvania.

1897. Rhein, John H. W., M.D., Neurologist to the Howard Hospital; Physician to the Philadelphia Home for Incurables; Bacteriologist to the Pennsylvania Training School for Feeble-minded Children; Member of the American Neurological Association. 1732 Pine St.

1906. Rhein, Robert D., M.D., Associate Physician to the American Hospital for Diseases of the Stomach; Examining Physician to the Free Hospital for Poor Consumptives, White Haven, Pa. 2016 Pine St.

1891. Rhoads, Edward G., M.D. 159 W. Coulter St., Germantown.

ELECTED

1898. Riesman, David, M.D., Professor of Clinical Medicine in the Philadelphia Polyclinic; Assistant Professor of Medicine in the University of Pennsylvania; Physician to the Philadelphia General and the Jewish Hospitals. 1715 Spruce St.

1895. Ring, G. Oram, A.M., M.D., Ophthalmic Surgeon to the Episcopal Hospital; Ophthalmologist to the Widener Memorial Home for Crippled Children; Consulting Ophthalmologist to the American Oncologic Hospital. 2014 Chestnut St.

1905. Risley, J. Norman, M.D., Assistant Surgeon to the Wills Eye Hospital; Ophthalmologist to the Pennsylvania Training School for Feeble-minded Children. 1728 Chestnut St.

1891. Risley, S. D., M.D., Attending Surgeon to the Wills Eye Hospital; Professor (Emeritus) of Ophthalmology in the Philadelphia Polyclinic and College for Graduates in Medicine; Member of the Board of Managers of the Pennsylvania Training School for Feeble-minded Children; Alumnus Manager of the University Hospital. 1728 Chestnut St.

†1878. Roberts, John B., M.D., Professor of Surgery in the Philadelphia Polyclinic; Surgeon to the Methodist Episcopal Hospital. 313 S. Seventeenth St.

1899. Roberts, Walter, M.D., Professor of Otology in the Philadelphia Polyclinic; Otologist to the Methodist Episcopal Hospital; Laryngologist to the Philadelphia General Hospital. 1732 Spruce St.

1903. Robertson, William Egbert, M.D., Physician to the Episcopal Hospital; Professor of the Theory and Practice of Medicine in Temple University; Physician to the Samaritan and the Garretson Hospitals. 320 S. Sixteenth St.

1907. Robinson, Edwin Taylor, M.D. 1906 Pine St.

1902. Robinson, James Weir, M.D., Assistant Surgeon to the Presbyterian Hospital. 326 S. Sixteenth St.

1903. Robinson, William Duffield, Ph.G., M.D. 2012 Mount Vernon St.

1900. Rodman, William L., M.D., Professor of Surgery in the Medico-Chirurgical College; Surgeon to the Presbyterian Hospital; Surgeon to the Philadelphia General Hospital. 1904 Chestnut St.

1909. Rosenberger, Randle C., M.D., Professor of Hygiene and Bacteriology in the Jefferson Medical College; Direc-

ELECTED

tor of the Clinical Laboratory of the Philadelphia General Hospital; Lecturer on Hygiene in the Woman's Medical College of Pennsylvania; Bacteriologist to the Jefferson Medical College Hospital. 2330 N. Thirteenth St.

1898. Ross, George G., M.D., Assistant Surgeon to the German Hospital and Surgeon to the Out-patient Department of the same; Surgeon to the Germantown Hospital. 1721 Spruce St.

*1907. Royer, B. Franklin, M.D. Donaldson Building, Harrisburg, Pa.

†1905. Rugh, James Torrance, M.D., Orthopedic Surgeon to the Methodist Hospital; Demonstrator of Orthopedic Surgery in the Jefferson Medical College; Assistant Orthopedist to the Jefferson Hospital; Assistant Orthopedist to the Philadelphia General Hospital. 1616 Spruce St.

1897. Sailer, Joseph, M.D., Associate in Medicine in the University of Pennsylvania; Associate of the Pepper Clinical Laboratory of the University of Pennsylvania; Pathologist to the Pennsylvania Training School for Feeble-minded Children. 1830 Spruce St.

1900. Sajous, Charles E. de M., M.D., B.Lett., LL.D., Knight of the Legion of Honor, and Officer of the Academy of France; Corresponding Member of the Society of Public Medicine of Belgium; Member of Honor of the French Society of Hygiene, etc. 2043 Walnut St.

1905. Sartain, Paul J., M.D. 212 W. Logan Square.

1908. Sautter, Albert C., M.D., Assistant in the Dispensary for Diseases of the Eye in the University Hospital; Assistant in the Eye Dispensary of the German Hospital. 1421 Locust St.

1906. Saylor, Edwin S., M.D., Ophthalmologist to St. Timothy's Hospital, Roxborough. 2005 Chestnut St.

1899. Schamberg, Jay F., M.D., Professor of Dermatology and Infectious Eruptive Diseases in the Philadelphia Polyclinic and College for Graduates in Medicine; Assistant Physician to the Municipal Hospital for Infectious Diseases. 1922 Spruce St.

1907. Schwartz, George J., M.D., Assistant Surgeon to the Philadelphia General Hospital; Instructor in Surgery in Jefferson Medical College. 1633 S. Fifteenth St.

1887. Schweinitz, George E. de, M.D., Professor of Ophthalmol-

ELECTED

ogy in the University of Pennsylvania; Ophthalmic Surgeon to the Philadelphia General Hospital; Consulting Ophthalmic Surgeon to the Philadelphia Polyclinic; Ophthalmologist to the Orthopædic Hospital and Infirmary for Nervous Diseases. 1705 Walnut St.

1892. Seiss, Ralph W., M.D., Professor of Otology in the Philadelphia Polyclinic; Consulting Laryngologist to the Pennsylvania Institution for the Deaf and Dumb. 255 S. Seventeenth St.

1908. Shannon, Charles E. G., M.D., Instructor in Ophthalmology in the Jefferson Medical College; Assistant in the Ophthalmological Clinic at Jefferson Medical College Hospital. 2025 Chestnut St.

1897. Sharpless, William T., M.D., Physician to the Chester County Hospital. West Chester, Pa.

1906. Shields, William G., M.D., Chief of Dermatological Clinic and Assistant Physician to the Jewish Hospital. 412 School House Lane, Germantown.

1876. Shippen, Edward, A.M. (Princeton), M.D., Rear Admiral on the Retired List, U. S. Navy. 2039 Pine St.

1891. Shober, John B., A.M., M.D., Associate Gynecologist to the Gynecean Hospital; Gynecologist to the Howard Hospital; Obstetrician to the Philadelphia General Hospital. 1731 Pine St.

1890. Shoemaker, George Erety, A.M., M.D., Gynecologist to the Presbyterian Hospital and to the Pennsylvania Epileptic Hospital and Colony Farm; Consulting Surgeon to the Woman's Hospital of Philadelphia. 1831 Chestnut St.

1908. Shoemaker, Harlan, A.B. (Stanford), M.D., Pathologist to the Methodist Hospital. 1618 Spruce St.

†1893. Shoemaker, Harvey, M.D., Visiting Physician to the Sheltering Arms and to the Southern Home for Destitute Children; Assistant Physician to the German Hospital; Physician to the Out-patient Department of the German and the Pennsylvania Hospitals. 2011 Chestnut St.

†1896. Shoemaker, William T., M.D., Ophthalmic Surgeon to the Germantown Hospital; Assistant Ophthalmologist and a Chief of Clinic to the German Hospital; Dispensary Ophthalmic Surgeon to the Presbyterian Hospital; Consulting Ophthalmologist to the Pennsylvania Institution for the Deaf and Dumb. 2031 Chestnut St.

1900. Shumway, Edward Adams, B.S., M.D., Instructor in Oph-

ELECTED

thalmology in the University of Pennsylvania, and Assistant Ophthalmic Surgeon to the University Hospital; Assistant Ophthalmologist to the Philadelphia General Hospital; Assistant Ophthalmologist and a Chief of Clinic to the German Hospital. 2007 Chestnut St.

1903. Sinclair, John Falconer, M.D., Physician to the Medical Dispensary of the Presbyterian Hospital; Physician to the Philadelphia Orphan Asylum and to the Presbyterian Orphanage; Physician to the Home of the Merciful Saviour for Crippled Children. 4103 Walnut St.

1907. Sinkler, Francis Wharton, A.B., M.D., Assistant Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases; Physician to the Episcopal Hospital. 220 S. Sixteenth St.

1872. Sinkler, Wharton, M.D., Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases; Neurologist to the State Asylum for the Chronic Insane of Pennsylvania. 1606 Walnut St.

1902. Siter, E. Hollingsworth, M.D., Instructor in Genito-urinary Diseases in the University of Pennsylvania; Genito-urinary Surgeon to the Philadelphia General Hospital; Surgeon-in-Charge of the Genito-urinary Dispensary of the University Hospital; Surgeon to the Dispensary of the Children's Hospital. 2038 Locust St.

1904. Skillern, Penn Gaskill, M.D. 241 S. Thirteenth St.

1904. Smith, Allen J., M.D., Professor of Pathology in the University of Pennsylvania; Pathologist to the University Hospital, to the Philadelphia General Hospital, and to the State Hospital for the Insane at Norristown, Pa. University of Pennsylvania.

1905. Smith, S. MacCuen, M.D., Professor of Otology in the Jefferson Medical College; Aurist and Laryngologist to the Germantown Hospital; Aurist to the Jewish Hospital; Consulting Aurist to the Oncologic Hospital. 1429 Spruce St.

1908. Speese, John, M.D., Assistant Instructor in Surgery in the University of Pennsylvania; Surgeon to the Dispensary of the University and the Children's Hospitals. 248 S. Twenty-first St.

1895. Spellissy, Joseph M., A.M., M.D., Surgeon to the Outpatient Department of the Pennsylvania Hospital; Visiting Surgeon to St. Joseph's and to the Methodist Episcopal Hospitals; Assistant Surgeon to the Orthopædic Department of the University Hospital. 110 S. Eighteenth St.

ELECTED

1897. Spiller, William G., M.D., Associate Professor of Neurology and Professor of Neuropathology in the University of Pennsylvania; Clinical Professor of Nervous Diseases in the Woman's Medical College of Pennsylvania; Professor of Nervous Diseases in the Philadelphia Polyclinic and College for Graduates in Medicine. 4409 Pine St.

1908. Spitzka, Edward Anthony, M.D., Professor of General Anatomy in the Jefferson Medical College. Jefferson Medical College.

1894. Stahl, B. Franklin, B.S., Ph.G., M.D., Clinical Professor of Medicine in the Woman's Medical College of Pennsylvania; Lecturer on Dietetics of the Sick and Instructor in Physical Diagnosis in the University of Pennsylvania; Visiting Physician to St. Agnes' Hospital; Visiting Physician to the Philadelphia General Hospital. 1727 Pine St.

1904. Stanton, William B., M.D., Physician to the Department of Tuberculosis, Philadelphia General Hospital; Physician to the Henry Phipps Institute; Visiting Physician to the Free Hospital for Poor Consumptives, White Haven, Pa. 732 Pine St.

1909. Starbuck, J. Clinton, M.D. 42 E. Washington St., Media, Pa.

1875. Starr, Louis, M.D., LL.D. (Haverford). 1818 S. Rittenhouse Square.

1892. Steinbach, Lewis W., M.D., Professor of Clinical and Operative Surgery in the Philadelphia Polyclinic; Visiting Surgeon to the Philadelphia General and the Jewish Hospitals. 1309 N. Broad St.

1884. Stelwagon, Henry W., M.D., Ph.D., Professor of Dermatology in the Jefferson Medical College; Dermatologist to the Philadelphia General and the Howard Hospitals; Associate Member of the Society of Dermatology and Syphilology of France and of Italy. 1634 Spruce St.

1895. Stengel, Alfred, M.D., Professor of Clinical Medicine in the University of Pennsylvania; Physician to the University, the Pennsylvania, and the Philadelphia General Hospitals. 1811 Spruce St.

1901. Stevens, Arthur A., M.D., Professor of Materia Medica, Therapeutics, and Clinical Medicine in the Woman's Medical College of Pennsylvania; Lecturer on Physical Diagnosis in the University of Pennsylvania; Physician to the Episcopal and St. Agnes' Hospitals. 314 S. Sixteenth St.

ELECTED

1902. Stewart, Francis T., M.D., Professor of Surgery in the Philadelphia Polyclinic and College for Graduates in Medicine; Surgeon to the Germantown Hospital; Assistant Surgeon to the Jefferson Medical College Hospital; Surgeon to the Out-patient Department of the Pennsylvania Hospital. 311 S. Twelfth St.

1898. Stout, George C., M.D., Professor of Otology in the Philadelphia Polyclinic and College for Graduates in Medicine; Laryngologist and Aurist to the Presbyterian Hospital, the Children's Aid Society, and the William Penn Charter School. 1611 Walnut St.

1884. Stryker, Samuel S., M.D., Physician to the Presbyterian Hospital. 3833 Walnut St.

1900. Swan, John M., M.D., Associate Professor of Clinical Medicine in the Medico-Chirurgical College of Philadelphia; Assistant Physician to the Medico-Chirurgical Hospital; Instructor in Clinical Pathology and in Tropical Medicine in the Philadelphia Polyclinic and College for Graduates in Medicine; Secretary of the American Society of Tropical Medicine. 3713 Walnut St.

1898. Sweet, William M., M.D., Professor of Diseases of the Eye in the Philadelphia Polyclinic; Associate Professor of Ophthalmology in the Jefferson Medical College; Assistant Ophthalmic Surgeon to the Philadelphia General Hospital; Consulting Ophthalmologist to the Phœnixville Hospital. 1205 Spruce St.

1906. Tait, Thomas W., M.D., Ophthalmologist to St. Agnes' Hospital and to the Charity Hospital. 320 S. Fifteenth St.

1900. Talley, James Ely, A.B., M.D., Physician to the Presbyterian Hospital. 1927 Chestnut St.

1901. Taylor, J. Gurney, M.D., Physician to the Pennsylvania Institution for the Instruction of the Blind. 6041 Drexel Road, Overbrook, Pa.

1886. Taylor, John Madison, A.M. (Princeton), M.D., Editor *Monthly Cyclopedia of Practical Medicine;* Pediatric Physician to the Philadelphia General Hospital; Assistant Physician to the Children's Hospital; Consulting Physician to the Elwyn, Pa., and the Vineland, N. J., Training Schools for Feeble-minded Children. 1504 Pine St.

1887. Taylor, William J., M.D., Surgeon to the Orthopædic Hospital and Infirmary for Nervous Diseases, and to St. Agnes'

ELECTED

Hospital; Consulting Surgeon to the West Philadelphia Hospital for Women. 1825 Pine St.

1886. Taylor, William L., M.D. 1340 N. Twelfth St.

1867. Thomas, Charles Hermon, M.D. 3634 Chestnut St.

1907. Thomas, Thomas Turner, M.D., Instructor in Surgery in the University of Pennsylvania; Assistant Surgeon to the University Hospital; Assistant Surgeon to the Philadelphia General Hospital. 2005 Chestnut St.

1897. Thomson, A. G., M.D., Assistant Ophthalmic Surgeon to the University Hospital; Assistant Ophthalmologist to the Orthopædic Hospital and Infirmary for Nervous Diseases. 1426 Walnut St.

1896. Thorington, James, A.M., M.D., Professor of Diseases of the Eye in the Philadelphia Polyclinic; Member of the American Ophthalmological Society; Ophthalmologist to the Vineland and Elwyn Training Schools for Feeble-minded Children. 120 S. Eighteenth St.

1898. Thornton, Edward Q., M.D., Assistant Professor of Materia Medica in the Jefferson Medical College. 922 Spruce St.

1896. Toulmin, Harry, M.D., Assistant Medical Director of the Penn Mutual Life Insurance Company. 925 Chestnut St.

1908. Tracy, Stephen E., M.D., Gynecologist to the Stetson Hospital. 1429 Spruce St.

1901. Tucker, Henry, M.D. 2000 Pine St.

†1894. Tunis, Joseph Price, M.D., Clinical Assistant to the Nose and Throat Dispensary of the Polyclinic Hospital. 1426 Pine St.

1901. Turner, John B., M.D., Clinical Assistant in the Ophthalmological Out-patient Department of the Jefferson Medical College Hospital. 1833 Chestnut St.

1866. Tyson, James, M.D., LL.D., Professor of Medicine in the University of Pennsylvania and Physician to the Hospital of the University of Pennsylvania; Physician to the Pennsylvania Hospital. 1506 Spruce St.

1897. Tyson, T. Mellor, M.D., Physician to the Philadelphia General Hospital; Assistant Physician to the Hospital of the University of Pennsylvania; Physician to the Rush Hospital, the Philadelphia Lying-in Charity Hospital, and the Children's Aid Society of Philadelphia. 1506 Spruce St.

1904. Uhle, Alexander A., M.D., Assistant Instructor in Genito-urinary Diseases in the University of Pennsylvania;

ELECTED

Assistant Surgeon to the Dispensary for Genito-urinary Diseases, University Hospital; Assistant Genito-urinary Surgeon to the Philadelphia General Hospital; Assistant Surgeon to the Dispensary of the German Hospital. 1327 Jefferson St.

1907. Ullom, Josephus Tucker, A.B., M.D., Member of the Staff of the Henry Phipps Institute for Tuberculosis. 24 Carpenter St., Germantown.

1873. Van Harlingen, Arthur, Ph.B. (Yale), M.D., Emeritus Professor of Diseases of the Skin in the Philadelphia Polyclinic; Dermatologist to the Children's Hospital. 1831 Chestnut St.

1903. Van Pelt, William Turner, M.D., Ophthalmic Surgeon to the Episcopal Hospital. 1528 Spruce St.

1893. Vansant, Eugene Larue, M.D., Professor of Diseases of the Throat and Nose in the Philadelphia Polyclinic; Visiting Physician to the Throat, Nose, and Ear Department of the Howard Hospital. 1929 Chestnut St.

*1897. Veasey, Clarence A., A.M., M.D., Formerly Assistant Professor of Ophthalmology in the Jefferson Medical College, and Assistant Ophthalmologist to the Jefferson Medical College Hospital; Formerly Ophthalmic Surgeon to the Methodist Episcopal Hospital, Philadelphia. Suite 205, Traders' Bank Building, Spokane, Wash.

†1883. Vinton, Charles Harrod, M.D. Wernersville, Berks County, Pa.

1903. Wadsworth, William Scott, M.D. The Normandie, Thirty-sixth and Chestnut Sts.

1885. Walker, James B., M.D., Ph.D., Consulting Physician to the West Philadelphia Hospital for Women and Children. 1617 Green St.

1906. Walker, John K., M.D., Physician to the Out-patient Department of the Pennsylvania Hospital; Physician to the Dispensary of the Mary J. Drexel Home. 1632 Spruce St.

1907. Walker, Warren, M.D., Surgeon to the Dispensary of the Episcopal Hospital; Surgeon to the Dispensary of the Children's Hospital; Assistant Surgeon in the Clinic for Genito-urinary Diseases of the Polyclinic Hospital. 1632 Spruce St.

ELECTED

1904. Walsh, Joseph, A.M., M.D., Physician to the Henry Phipps Institute; Visiting Physician to the White Haven Sanatorium; Physician to the Department of Tuberculosis at the Philadelphia General Hospital. 732 Pine St.

1893. Warren, Joseph W., M.D., Associate Professor of Physiology in Bryn Mawr College. Bryn Mawr, Pa.

1895. Watson, Arthur W., M.D., Professor of Diseases of the Throat and Nose in the Philadelphia Polyclinic and College for Graduates in Medicine; Laryngologist to the Jewish Hospital; Laryngologist and Aurist to the Mt. Sinai Hospital; Laryngologist to the Home for Incurables. 126 S. Eighteenth St.

1886. Watson, Edward W., M.D., Physician to the Magdalene Home. 38 S. Nineteenth St.

1903. Weber, Charles H., M.D., Physician to the Episcopal Hospital; Physician to the Dispensary of the Children's Hospital. 1304 Pine St.

1906. Weisenburg, Theodore H., M.D., Professor of Neuropathology and Associate Professor of Neurology in the Medico-Chirurgical College; Neurologist to the Philadelphia General Hospital; Consulting Neurologist to the State Hospital for the Insane at Norristown and to the State Hospital for the Feeble-minded and Epileptic at Spring City. 2030 Chestnut St.

1883. Welch, William M., M.D., Chief Diagnostician to the Bureau of Health, and Consulting Physician to the Municipal Hospital for Contagious Diseases; Consulting Physician to the Northern Dispensary and the Northern Home for Friendless Children. 1411 Jefferson St.

1897. Wells, William H., M.D., Associate in Obstetrics in the Jefferson Medical College; Assistant Obstetrician to the Jefferson Medical College Hospital. 1105 Spruce St.

1893. Westcott, Thompson S., M.D., Associate in Diseases of Children in the University of Pennsylvania; Visiting Physician to the Methodist Episcopal Hospital; Assistant Physician to the Children's Hospital; Pediatrist to the Jewish Hospital. 1720 Pine St.

1884. Wharton, Henry R., M.D., Clinical Professor of Surgery in the Woman's Medical College of Pennsylvania; Surgeon to the Presbyterian and the Children's Hospitals; Consulting Surgeon to the Bryn Mawr Hospital, St. Christopher's Hospital for Children, and the Pennsylvania Institution for the Deaf and Dumb. 1725 Spruce St.

ELECTED

1901. White, Courtland Y., M.D., Lecturer on and Demonstrator of Gross Morbid Anatomy in the Veterinary Department of the University of Pennsylvania; Pathologist to the State Live Stock Sanitary Board, the Children's, and St. Joseph's Hospitals; Pathological Director at the Episcopal Hospital. 1808 Diamond St.

1878. White, J. William, M.D., Ph.D., LL.D. (Hon. Aberdeen). John Rhea Barton Professor of Surgery in the University of Pennsylvania; Senior Surgeon to the University Hospital; Fellow of the American Surgical Association and of the American Association of Genito-urinary Surgeons. 1810 S. Rittenhouse Square.

1905. Whiteway, Harold M., M.D. 1924 Chestnut St.

1898. Whiting, Albert D., M.D., Surgeon to the Germantown Hospital; Assistant Surgeon to the German Hospital; Surgeon to the Southern Home for Destitute Children; Surgeon to the Out-patient Department of the German Hospital. 1523 Spruce St.

†1880. Willard, De Forest, A.M., M.D., Ph.D., Professor of Orthopedic Surgery in the University of Pennsylvania; Surgeon-in-Chief to the Widener School; Consulting Surgeon to the Presbyterian, the Germantown, the Jewish, the Atlantic City, and the Phœnixville Hospitals. 1901 Chestnut St.

1907. Williams, Carl, B.S., M.D., Assistant Ophthalmic Surgeon to the Germantown Hospital; Assistant Surgeon to the Dispensary for Diseases of the Eye at the University Hospital. N. E. cor. Schoolhouse Lane and Greene St., Germantown.

1902. Willson, Robert N., Jr., M.D., Pathologist to the Presbyterian Hospital; Assistant Physician to the Philadelphia General Hospital. 1708 Locust St.

1881. Wilson, H. Augustus, M.D., Professor of Orthopedic Surgery in the Jefferson Medical College; Emeritus Professor of Orthopedic Surgery in the Philadelphia Polyclinic; Consulting Orthopedic Surgeon to the Philadelphia Lying-in Charity Hospital, and the Kensington Hospital for Women; Senior Orthopedic Surgeon to the Philadelphia General Hospital. 1611 Spruce St.

1874. Wilson, James C., A.M. (Princeton), M.D., Professor of the Practice of Medicine and of Clinical Medicine in the Jefferson Medical College, and Physician to the Hospital of the same (Faculty Staff); Physician-in-Chief to the German

ELECTED

Hospital; Attending Physician to the Pennsylvania Hospital. 1509 Walnut St.

1902. Wilson, Samuel M., M.D. 1517 Arch St.

1897. Wilson, W. Reynolds, M.D., Visiting Physician to the Philadelphia Lying-in Charity Hospital. 1709 Spruce St.

1904. Wister, James W., M.D., Physician to the Out-patient Department of the Germantown Hospital. 5430 Germantown Ave.

*1901. Witmer, A. Ferree, M.D. Freeport, Long Island, N. Y.

1893. Wood, Alfred C., M.D., Assistant Professor of Surgery in the University of Pennsylvania; Assistant Surgeon to the University Hospital; Surgeon to the Philadelphia General and St. Timothy's Hospitals. 128 S. Seventeenth St.

1900. Wood, George B., M.D., Instructor in Laryngology in the University of Pennsylvania; Assistant in the Clinic for Diseases of the Nose and Throat at the Polyclinic Hospital. 129 S. Eighteenth St.

1865. Wood, Horatio C., M.D., LL.D. (Yale and Lafayette), Emeritus Professor of Materia Medica and Therapeutics in the University of Pennsylvania; Associate Fellow in Medicine and Surgery of the American Academy of Arts and Sciences; Member of the National Academy of Science. 4107 Chester Ave.

1903. Wood, Horatio C., Jr., M.D., Associate Professor of Pharmacology in the University of Pennsylvania. 434 S. Forty-fourth St.

1907. Wood, Walter A., M.D. 1715 Spruce St.

1880. Woodbury, Frank, M.D., Secretary to the Committee on Lunacy of the Board of Charities of Pennsylvania. 218 S. Sixteenth St.

1866. Woods, D. F., M.D., Physician to the Presbyterian Hospital. 1501 Spruce St.

1901. Woods, Richard F., M.D., Assistant Surgeon to the Gynecean Hospital. 1501 Spruce St.

†1897. Woodward, George, M.D. W. Willow Grove Ave., Chestnut Hill, Philadelphia.

1903. Worden, Charles B., M.D., Associate in Diseases of the Stomach and Intestines in the Philadelphia Polyclinic; Physician to the Dispensary of the Presbyterian Hospital; Anesthetizer to the Orthopedic Department of the University Hospital; Physician to the Presbyterian Orphanage. 322 S. Sixteenth St.

ELECTED

1889. YOUNG, JAMES K., M.D., Professor of Orthopedic Surgery in the Philadelphia Polyclinic; Clinical Professor of Orthopedic Surgery in the Woman's Medical College of Pennsylvania; Associate in Orthopedic Surgery in the University of Pennsylvania, and Assistant Orthopedic Surgeon to the University Hospital. 222 S. Sixteenth St.

1894. ZENTMAYER, WILLIAM, M.D., Attending Surgeon to the Wills Eye Hospital; Ophthalmic Surgeon to St. Agnes' Hospital; Ophthalmologist to the House of Refuge. 1819 Spruce St.

1899. ZIEGLER, S. LEWIS, A.M., M.D., Sc.D., Attending Surgeon to the Wills Eye Hospital; Ophthalmic Surgeon to St. Joseph's Hospital; Membre Société Française d'Ophtalmologie. 1625 Walnut St.

1887. ZIEGLER, WALTER M. L., A.M., M.D. 1418 N. Seventeenth St.

1895. ZIMMERMAN, MASON W., M.D., Consulting Ophthalmic Surgeon to the Germantown Hospital. 1522 Locust St.

ASSOCIATE FELLOWS.

[Limited to Fifty, of whom Twenty may be Foreigners.]

American.

ELECTED

1909. Billings, Frank, M.D., 335 E. Twenty-second Street, Chicago, Illinois.

1876. Billings, John S., M.D., U. S. A., Astor Library Building, 40 Lafayette Place, New York City, New York.

1886. Bowditch, Henry P., M.D., 688 Boylston Street, Boston, Massachusetts.

1877. Chaille, Stanford E., M.D., University Building, New Orleans, Louisiana.

1886. Cheever, David W., M.D., 557 Boylston Street, Boston, Massachusetts.

1893. Councilman, William T., M.D., Harvard Medical College, Boston, Massachusetts.

1909. Crile, George W., M.D., 1021 Prospect Avenue, S. E., Cleveland, Ohio.

1909. Dana, Charles Loomis, M.D., 53 West Fifty-third Street, New York City, New York.

1892. Emmet, Thomas Addis, M.D., 91 Madison Avenue, New York City, New York.

1892. Fitz, Reginald H., M.D., 81 Arlington Street, Boston, Massachusetts.

1895. Fletcher, Robert, M.D., Army Medical Museum, Washington, D. C.

1903. Gorgas, William C., M.D., U. S. A., Washington, D. C.

1891. Jacobi, A., M.D., 19 East Forty-seventh Street, New York City, New York.

1909. Janeway, Edward G., M.D., LL.D., 36 West Fortieth Street, New York City, New York.

1895. McBurney, Charles, M.D., 28 West Thirty-seventh Street, New York City, New York.

ELECTED

1909. Macallum, Archibald B., M.A., M.B., Ph.D., Sc.D., LL.D., F.R.S., 59 St. George Street, Toronto, Canada.
1909. Mall, Franklin P., M.D., 1514 Bolton Street, Baltimore, Maryland.
1906. Mayo, William J., M.D., Rochester, Minnesota.
1906. Pilcher, Lewis Stephen, M.D., 386 Grand Avenue, Brooklyn, New York.
1886. Reeve, John C., M.D., LL.D., S. W. corner Third and Wilkinson Streets, Dayton, Ohio.
1906. Shattuck, Frederick C., M.D., 135 Marlborough Street, Boston, Massachusetts.
1896. Sternberg, George M., M.D., U. S. A., 1019 Sixteenth Street N. W., Washington, D. C.
1896. Tiffany, L. McLane, M.D., 831 Park Avenue, Baltimore, Maryland.
1909. Wadsworth, Oliver F., M.D., 526 Beacon Street, Boston, Massachusetts.
1894. Warren, J. Collins, M.D., 58 Beacon St., Boston, Massachusetts.
1894. Weir, Robert F., M.D., 11 East Fifty-fourth Street, New York City, New York.
1892. Welch, William H., M.D., Johns Hopkins Hospital, Baltimore, Maryland.

Foreign.

1890. Baccelli, Guido, Rome, Italy.
1908. Bannerman, W. B., M.D., Lt. Col. I. M. S., 11 Strathearn Place, Edinburgh, Scotland.
1894. Brunton, Sir T. Lauder, M.D., 10 Stratford Place, London, W., England.
1903. Finlay, Charles J., M.D., Havana, Cuba.
1899. Fraser, Sir Thomas R., M.D., LL.D., F.R.C.P., F.R.S., 13 Drumsheigh-Gardens Edinburgh, Scotland.
1903. Horsley, Sir Victor Alexander Haden, F.R.S., 25 Cavendish Square, London, England.
1906. Hutchinson, Jonathan, M.D., LL.D., F.R.S., 15 Cavendish Square, London, W., England.
1896. Jaccoud, Prof. S., Rue Tronchet 35, Paris, France.
1894. Jackson, J. Hughlings, M.D., 3 Manchester Square, London, England.
1893. von Jaksch, Rudolf, M.D., Prague, Bohemia.

ELECTED.

1903. Kocher, Prof. Theodor, M.D., Berne, Switzerland
1896. Leyden, Ernst, M.D., Berlin, Germany.
1877. Lord Lister, M.D., LL.D., F.R.S., 12 Park Crescent, Portland Place, London, W., England.
1906. Myles, Sir Thomas, M.D., 33 Merion Square, W., Dublin, Ireland.
1896. Pye-Smith, P. H., M.D., 48 Brook St., London, W., England.
1898. Roddick, Thomas G., M.D., 80 Union Avenue, Montreal, Canada.
1908. Ross, Major Ronald, M.D., R.A., Liverpool School of Tropical Medicine, Liverpool, England.
1869. Valcourt, Th. de, M.D., Cannes, France.
1904. Waldeyer, Prof. Wilhelm, M.D., Berlin, Germany.

CORRESPONDING MEMBERS.

ELECTED

1880. Carrow, Flemming, M.D., Washington Arcade, Detroit, Michigan.

1880. Chiara, Domenico, M.D., Florence, Italy.

1886. Dey, Kanny Lall, M.D., Calcutta, India.

1885. Rendu, Jean, M.D., Lyons, France.

NECROLOGICAL LIST.

FELLOWS.

R. A. F. PENROSE,	December, 26, 1908
HARRY GODEY,	January 30, 1909
J. ALISON SCOTT,	August 13, 1909
HENRY C. CHAPMAN,	September 8, 1909
GEORGE C. HARLAN,	September 25, 1909
JOHN JANVIER BLACK (n. r.),	September 27, 1909

ASSOCIATE FELLOW.

PHINEAS SANBORN CONNER,	March 26, 1909

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MEMOIR OF JOHN HOOKER PACKARD, M.D.[1]

By JOHN H. GIBBON, M.D.

A REVIEW of the life of any man who has achieved success and honor in his particular calling is always a pleasure, especially to those who find themselves pursuing the same line of work; and if what is said of Dr. Packard prove uninteresting, it is only the fault of his biographer, for not only did he gain success and honor in medicine, but he was a man who possessed other qualities which make a study of his life entertaining.

John Hooker Packard was born in Philadelphia, Pa., August 15, 1832, and died in Atlantic City, New Jersey, May 21, 1907, at the age of seventy-five. His ancestors were all Puritans of the bluest stocking. He was a direct descendant of that Thomas Hooker who founded the town of Springfield with a large number of Congregationalists whom he took with him from Boston. Among the distinguished New England names that figure in his ancestry are those of Hooker, Quincy, and Dwight. Dr. Packard's father was a lawyer who removed to Philadelphia from Springfield and interested himself very largely in philanthropic work. It was his custom to deliver addresses at regular intervals to the pupils at Girard College. Ministers of all denominations being denied entrance to this institution, Mr. Packard was selected because of his devout and upright life to direct the moral training of the students.

It has ever been too much the custom of the biographer in reviewing the life of his subject to hold him up to the living as an absolutely spotless example of all that is virtuous, or else to detract from the writings of some other biographer by presenting only the unpleasant

[1] Read January 6, 1909.

and evil side of the subject's character. In dealing with Dr. Packard I shall endeavor to place him before you as he ever placed himself, a quiet, modest, conscientious gentleman.

Dr. Packard was graduated from the Department of Arts of the University of Pennsylvania in 1850. He then entered the Medical School of the University of Pennsylvania, from which he was graduated in 1853. He started the study of medicine under the very best auspices, having as his preceptor the distinguished Joseph Leidy, to whose teaching he undoubtedly owed his fondness for and skill in anatomical pursuits, which distinguished him throughout his professional career. Having graduated in medicine, he went abroad for the purpose of completing his medical education, and spent most of his time in Paris. His sketches and diaries of this period are interesting and very amusing. His diary shows that the time in Paris was well spent, being devoted much more to work than to the pursuit of those pleasures for which the French capital has always been so noted, and which the American medical student has always found it difficult to forego. He did a great deal of dissection, took a course in microscopy, and attended regularly the clinics at the different hospitals. He notes several operations which he saw performed by the great Nélaton.

On his return to America, in 1855, he was elected a Resident Physician at the Pennsylvania Hospital, in which capacity he served for eighteen months. In starting the practice of his profession he immediately became engaged in teaching at the University of Pennsylvania and devoted himself particularly to anatomy, surgery, and obstetrics. As a teacher he was popular, and possessed that necessary quality of being able to impart his knowledge to his students. For a number of years he held the position of Demonstrator of Anatomy at the University. During the Civil War he was appointed Acting Assistant Surgeon in the United States Army, and served as Attending Surgeon to the Christian Street and the Satterlee Hospitals in Philadelphia. He also acted as Consulting Surgeon to the Haddington Hospital and to the Hospital at Beverly, New Jersey. During the progress of the battle of Gettysburg he received orders to report at the scene of action, and although quite ill at the

time from what subsequently developed into a very severe attack of typhoid fever, he obeyed at once. For three days and nights he labored incessantly, and then, being utterly unable to continue at work, was sent back to Philadelphia suffering from a nearly fatal attack of typhoid.

In 1863 he was elected Surgeon to the Episcopal Hospital, in which capacity he served for nineteen years, resigning when he was elected Surgeon to the Pennsylvania Hospital in 1884. This latter position he held until his retirement from active professional work in 1896. For a number of years he was also Surgeon to St. Joseph's Hospital. He was elected a Fellow of the College of Physicians in 1858, and served as its Secretary from 1862 to 1877 and as Vice-President from 1885 to 1888. He had the honor of being the first Mütter lecturer, delivering a number of interesting lectures on Inflammation, which were published in 1865. He also had the distinction of being one of the Founders of the Philadelphia Academy of Surgery, and of the Pathological and Obstetrical Societies. Of the two latter he was twice President. He was one of the Original Fellows of the American Surgical Association, and for two years was its Treasurer.

Dr. Packard's contributions to surgical literature have been many, varied, and valuable. In 1859 he published a translation of Malgaigne's *Treatise on Fractures*. In 1863 he published a *Handbook of Minor Surgery*, which was authorized and approved by the Surgeon-General for the use of surgeons in the field and in army hospitals. He also published a *Handbook of Operative Surgery* in 1870. For Ashhurst's *International Encyclopedia of Surgery*, published in 1883, he contributed the articles on "Poisoned Wounds" and on "Fractures," and in Keating's *Cyclopedia of the Diseases of Children*, published in 1889, he wrote the chapters on "Fractures and Dislocations." In 1881 he edited the American edition of Holmes' *System of Surgery*. He also published three editions of the *Philadelphia Medical Directory*, in 1868, 1871, and 1873. Among the articles which he has contributed to surgical literature several deserve special mention. In a paper published in 1872 he called attention to the primary stage of ether anesthesia,

during which many slight operations might be performed with impunity. In 1880, in another paper, he described his oblique incision of the skin for the purpose of lessening the amount of scar tissue in the healed wound. In 1886 he read before the Medico-legal Society of New York a paper in which he suggested the use of a lethal chamber for the infliction of the death penalty, death to be caused by the extraction of oxygen from the atmosphere and the introduction of carbonic acid gas. He was particularly interested in the radical cure of hernia, and presented several valuable papers on this subject.

He was much in demand as an expert in medico-legal cases, because of his knowledge, experience, and honesty, which qualities seem to have been more in demand in an expert then than now. Among the most famous trials in which he was thus employed were those of Parr, the Philadelphia murderer, and of Barclay Leak, of Burlington, New Jersey.

Dr. Packard possessed profound religious convictions, and served as a vestryman in several of the Episcopal churches of Philadelphia. Although a distinctly religious man, he rarely talked upon religious topics, but his belief was a vital part of his existence and colored all the important actions of his life.

His literary attainments made him a most agreeable companion. He had a wonderful memory for names and faces, and could always recall the books which he had read and their most conspicuous characters. His wide reading and his extensive travels, together with his medical and artistic attainments, gave him a peculiar attraction. From his early youth he showed considerable ability at drawing, and all his note-books at college and his diaries since are filled with telling sketches. From 1884 until his death he was a member of the Board of Directors of the Academy of the Fine Arts of Philadelphia, and served as Chairman of the Committee on Instruction from the year 1887 until his death.

He was a man of no mean ability in more than one art, and the possessor of those characteristics which create love and confidence. He had a keen sense of humor and was capable always of seeing the amusing and ridiculous side of a question. This tendency, it is

said, in his earlier days cost him friends, for nothing hurts like ridicule and caricature; but indulgence in this line was always due to his sense of the amusing, and not to any malice. You have probably all heard of the celebrated caricature which Dr. Packard made, when a student, of the late Dr. Hodge, who was Professor of Obstetrics at the University of Pennsylvania. On coming into his lecture room one morning and turning to the blackboard, Dr. Hodge was shocked to find it covered with a drawing which represented him mounted across a uterus into the mouth of which had been inserted a bit, at the reins of which he was desperately tugging. Underneath the picture was the legend, "Hodge on his Hobby." It is worthy of note that in later years Dr. Packard was Dr. Hodge's chief assistant.

To those of us who had the pleasure of serving under him in our hospital service he was always a kind and considerate chief, appreciative of our efforts, and always willing to give us a chance to show our budding abilities and to help us out of the difficult places. His hospital visits were sure to give pleasure aside from the strictly professional point of view, for who among the Residents does not remember his humorous reminiscences and his amusing pencil sketches? The latter were usually made while the Resident was waiting to be excused in order that he might go to dinner, which in those days was a mid-day function, and this fact somewhat detracted from one's appreciation of the sketches. It always seemed to the Resident Physicians of the Pennsylvania Hospital that their chiefs never stooped to anything so low as feeding themselves—certainly they did not observe the same meal hours as the Resident Staff. This evil in recent years has been somewhat ameliorated by the Resident politely inviting his chief to lunch.

It has been said that Dr. Packard was at times depressed and cynical, but this, I take it, was due to the fact that his words and not his actions were considered. An almost daily speech to his Resident before or after making the rounds in the wards was, "Well, doctor, I would like to have a million a year paid quarterly in advance." This, however, was never said in a complaining way, but was always accompanied by a merry twinkle of the eye.

In 1896 he had the misfortune to infect himself in the course of an operation, and because of this he was obliged a few years later to give up all active medical work. His death was ultimately caused by uremia, the result of cardiac insufficiency.

Dr. Packard was married to Elizabeth Wood, daughter of Charles S. Wood, and a niece of Dr. George B. Wood, on June 3, 1858. To them were born six children, one daughter and five sons, all of whom are now living with the exception of the late brilliant and distinguished Fellow of this College, Dr. Frederick A. Packard, who died in 1902.

Their home will always be remembered as most delightful, where one was sure to meet not only kind hospitality, but also charming and cultivated people.

Excepting for his unforutnate illness, which saddened his last ten years, Dr. Packard's life was a happy one, and he had that rare satisfaction of seeing each of his sons grow up to attain distinction in his individual calling, and to receive that same respect and confidence which had been given to himself.

MEMOIR OF WILLIAM THOMSON, M.D.[1]

By S. WEIR MITCHELL, M.D., F.R.S.,
CORRESPONDING MEMBER OF THE FRENCH ACADEMY OF MEDICINE.

All over the land statues, monuments, and tablets commemorate the services of generals and colonels in the Civil War. Nowhere is there a single public memorial of the surgeon, and yet, rank for rank, he lost by death and suffered proportionally as severely from wounds, sickness, imprisonment as officers of like rank in the line. This so-called non-combatant was never other than perilously busy in the epidemics of camps, and was needlessly often operating under fire. Private and general have told us their story. The doctor has been strangely silent, and has accepted the neglect of history. In the countless records of our great war his services are almost entirely without recognition.

We at least cannot afford to lose the thought of this memorable service; we of this College least of all. During the years of our great Civil War we had an average membership of 160 Fellows. Including a small number who became Fellows soon after the war, we gave to that great cause 129 physicians. Of these some fifty held commissions in the regular army or in the navy or in volunteer service. The remainder were acting assistant surgeons.

In this roll of honor stands high the subject of this memoir, William Thomson. He was born in Chambersburg, Pa., January 28, 1833, the son of Alexander Thomson, Judge of the Sixteenth Judicial District of the State, and Jane Graham, his wife. He was one of three sons, among whom was a younger brother, Frank Thomson, who as a major in the army was largely in charge of

[1] Read March 3, 1909.

most of the railroad transport of troops during the Civil War, and later, President of the Pennsylvania Railroad. Both brothers were examples of that fertile product of men of force so frequently found among the descendants of the Scotch-Irish Presbyterians whose ancestors settled, early in the eighteenth century, on the war line of the Alleghanies when the Indian was still formidable. In fact, one ancestor of Dr. Thomson perished in that savage warfare.

The child is not always the father of the man, but in the case of William Thomson he displayed as a boy the readiness he showed in after life to accommodate himself to circumstances and to overcome difficulties which would have defeated most children.

When about eight years old he suffered from a severe ulcer of his cornea, which confined him more or less for nearly two years to a darkened room, with treatment in the old-fashioned style by copper sulphate. During this time, not being able to use his eyes or to play outdoor sports with the other children, he spent much of his time at the piano, learning to play by ear. Music thus acquired was a source of great pleasure to him for the rest of his life, and he learned, then or later, to play by ear, and exceedingly well, the violin, piano, and flute.

His health became better after the disease of his eye had been cured, and he was able later to finish his school course. One characteristic of his after years as an investigator and inventor was shown at this early period. The ulcer of his eye most probably gave rise to a high hypermetropia. When he began again to use his eyes, he found difficulty in reading, as might be expected of a hypermetropia of five diopters; but thus early his inventive genius came to his aid. He discovered that by holding a candle between his eyes and the book, quite close to his eye, that he could read much more and with greater comfort. He read in this manner all of Scott's novels. It is easy to understand that the bright light close to the eye contracted his pupil, diaphragming the iris down, as it were, and thus making it easier to see to read.

After completing his academic education at Chambersburg Academy, he studied medicine at the Jefferson Medical College, and was graduated M.D. in 1853. He very early attracted the

attention of Dr. John Kearsley Mitchell, professor of the practice of medicine, and was led by him to take over the practice of Dr. Clark, of Merion, on the Pennsylvania Railroad, where he settled as a country physician. Four years later he married Miss Rebecca George, a member of a well-known family of Friends then living on the original grant of land from William Penn to their ancestor. This ample estate included George's Hill and other portions of Fairmount Park.

Dr. Thomson soon became the most trusted physician in and about Merion, and won the confidence of the summer residents so completely that he was frequently called on by them for advice during their winter abode in Philadelphia.

His position was assured, his professional income increasing, his future of prosperity full of promise. When, however, ten years after his graduation the great war broke out, his strong opinions as to the righteousness of the contest, together with a never satisfied ambition, decided him to abandon the certainties of peaceful practice for the insecure future of army life.

In the summer of 1861, as assistant surgeon, with rank as lieutenant, he entered the regular service, just before the disaster of Bull Run. He served in this position in the Army of the Potomac and in Washington and Alexandria until, in 1862, he joined General McClellan's headquarters as chief of staff to the medical director, Jonathan Letterman. He was present throughout the peninsula campaign and at Antietam.

Before Antietam, after the gallant fight at South Mountain, he was left in superior charge of a field where lay, dead or wounded, two thousand Union men and Confederates. In the light of this experience he proposed two reforms, which were at once adopted. These made a radical change in the character of field hospital supplies and led to the formation of division hospitals, to prevent any confusion during and after an engagement. These measures proved of such value in the Army of the Potomac that they were adopted throughout all the armies by order of the Secretary of War, and remained in force, with little or no change, until our forces were disbanded.

In 1863 he was placed as surgeon in charge of the Douglas Hospital, in Washington. He soon made it an acknowledged model of hospital efficiency, and found here, as elsewhere in war, a wide and varied field for his enterprising and industrious mind.

In 1864 he was made Medical Inspector at Washington, which contained in its various hospitals over 23,600 beds, and in which during that year 113,351 men were received, treated, and thence transported.

Early in 1866 he organized a hospital for the treatment of cholera, and had charge of the Post Hospital.

In 1866 he passed his second examination and was promoted to a captaincy, having already received brevets of captain and major for "faithful and meritorious service." After a brief stay on duty in Louisiana, he resigned in 1868 and was elected a Fellow of this College in April, 1869.

During his residence in Washington he was largely interested in the Army Medical Museum—the creation of another of our distinguished Fellows, John H. Brinton—and was the largest contributor to the first published catalogue, for which he wrote valuable descriptions of osteomyelitis and wounds of joints.

The very needful red-tape routine of hospitals, which so impaired the usefulness of many medical officers, did not lessen the constant mental enterprise of William Thomson. Having seen in the field and hospital how stumps and wounds became foul and covered with flies, he began to use freely creosote dressing. The flies no longer came and carried thence infection, the odors were controlled, and, observing very soon the bettered results in wounds thus treated, he used creosote constantly in all his dressings. He was somewhat puzzled, as I have heard him say, and surprised at the brilliant results thus obtained by the use of what is now one of our best disinfectants. Had he continued after the war to practise surgery, he would, I believe, have studied the causes of the success creosote had given him in the treatment of wounds, and, with his tendency to investigation, might have anticipated the greatest triumph of modern surgery.

As from time to time I saw his wards, I was struck with the

small and large inventions in the way of splints and dressings. My brother Edward, who was a medical cadet in the Douglas Hospital until his fatal illness, from diphtheria, said of this remarkable surgeon, that he had the most alert mind he had known in the medical service of the army.

With his friend William Norris he had utilized photography in the study of wounds, and had induced the Surgeon-General to establish, in connection with the Museum, a photographic bureau. Thomson and Norris were the first to make negatives by the wet process of the field of the microscope with high and low powers, and led the way to the splendid successes obtained later through the resources of the Surgeon-General's office. These studies in optics finally dominated the future of Thomson and Norris, and led to their practice and teaching of ophthalmic surgery.

Dr. Thomson, thus led by his mastery of photography to a close study of optics, began soon to display that facility of resource in ophthalmic medicine which characterized all he did. He had, too, the large experience in general practice which specialists too often lack, and for him the relation of the whole to a part of the body and of a part, as the eye, to the whole was never lost sight of.

In place of a return to Merion, he deliberately elected to settle amid men long in practice in Philadelphia. A short period of general practice dissatisfied him, and, with his enterprising hopefulness and extraordinary command of resources, he turned whither his tastes led, and told me, to my surprise, that he intended to practise only ophthalmic medicine. At that time this required courage, and, as some believed, training in Germany. The decision thus made was, however, not unwise, nor was he without unusual knowledge of optics.

I shall leave Professor de Schweinitz to relate what Dr. Thomson did for ophthalmology, but I may not lightly omit to speak of the work in which we were jointly concerned.

In 1861 Dr. Ezra Dyer, coming from Germany, with all the new knowledge of refraction, had settled in Philadelphia. I gave him his first case, and did what I could to sustain him against the prevalent sentiment then felt by our elders that a pure specialty had in

it something of charlatanism. When after the war Dr. Dyer became ill and thus fell out of practice, Dr. William Norris, then in Germany, had not begun his successful career. I was glad to find in Dr. Thomson a man whom I easily brought to believe in my previous discovery, that many headaches were due to defects in the eyes. My first papers owed much to Dr. Thomson.

For some years we had this interesting work to ourselves, and from the time I sent to him, as I had to Dr. Dyer, his first case, he continued to win results which placed him in the first rank of scientific students of the eye. The subject was in our early days delightfully fresh, and the constant novelty of the problems to be solved gave to these consultations the charm of original research. We were both teachers and taught, but to dwell on what we did were to say more of myself than seems to be here in place. A better critic and better informed man than I has pleased me by here doing for my friend what I am not competent to do. Dr. de Schweinitz writes as follows:

"All of Dr. Thomson's contributions to ophthalmology were good; those were best which were concerned with the influence, detection, and correction of the anomalies of the refraction of the eye and with the investigation of color blindness.

"How important his relation was to the discovery of the eye-strain reflexes—a discovery which, in so far as the relief of human suffering and the sum of human happiness are concerned, deserves to rank with the finest scientific announcements of the past century—is elsewhere described in this memoir. It has placed him in the front rank of those to whom ophthalmic science gladly accords its highest honors.

"Early in his career, Dr. Thomson's attention was directed to the subjective methods of determining the static refraction of the eye, and in 1870[1] he described a test for ametropia based on the experiment of Scheiner, and later in the same year[2] brought his method to the notice of the members of the American Ophthalmological Society. While the idea of utilizing the Scheiner experiment in this

[1] American Journal of the Medical Sciences, January, 1870.
[2] Transactions of the American Ophthalmological Society, 1870, p. 93.

respect was by no means a new one, the ingenuity and practicability of its application with the instrument which he had devised, and which consisted of four variously perforated brass disks, marked a distinct advance in methods of determining hyperopia and myopia, still further improved when three years later[1] he designed a fifth disk for the diagnosis and correction of astigmatism.

"Always anxious to improve his work and refine his methods, Dr. Thomson, in 1878,[2] returned to the methods of optometry based upon the measurement of the circles of diffusion and presented to his colleagues an instrument which he called an ametrometer, so constructed that by means of it a rapid and satisfactory detection of the anomalies of the refraction of the eye was possible. This apparatus was long favorably known and always has received in the best works on applied optics distinguished notice and full description.[3]

"In the years which followed, many instruments were devised for the rapid determination of the errors of refraction, some of the designers of which utilized Dr. Thomson's ideas without giving him the least credit. Partly for this reason doubtless, but chiefly because he believed he could improve upon his early work, in 1902[4] he brought before the American Ophthalmological Society a new apparatus for the correction of ametropia, and upon its constant improvement he spent much time during the last years of his life, working at it almost until the day of his death, with such success that one of the most competent judges of the value of such instruments in the practical work of ophthalmologists has said, 'Of the many instruments constructed in recent times for the purpose of estimating the refraction of the eye, and to which the name *refractometer* is usually applied, the best is the one devised by Dr. William Thomson.' In the work on this his last contribution to the ophthalmological armamentarium he was associated with his son, Dr. A. G. Thomson.

"No one more than Dr. Thomson recognized the necessity of

[1] Transactions of the American Ophthalmological Society, 1873, p. 83.

[2] Ibid., 1878, p. 455.

[3] The Refraction and Accommodation of the Eye, by E. Landolt, 1886, p. 249. J. B. Lippincott Company.

[4] Transactions of the American Ophthalmological Society, 1902, p. 512, and ibid., 1904.

accurately and fully correcting the errors of refraction, which by means of patient ingenuity he was so well enabled to detect, always with the aid of full mydriasis. A deep debt of gratitude is due to him in these respects: his early and constant insistence of the need that young myopes should wear the full correction of their refractive defects in order that the progression of the myopia should be checked; the important relation of astigmatism to the formation of the myopia crescent and the tendency of the myopia to increase; the need of painstaking investigation of conical cornea and the remarkable improvement in vision that high spherocylindrical combinations will often afford in this condition, far exceeding in value the uncertainties of operative interference. His views on these subjects were quietly stated many years before the knowledge of them became the common property of oculists.[1] He made no claims of priority; indeed, he had none to make. Others also thought about these matters, and wrote about them more conspicuously than he has done; but none more earnestly and few earlier, and when the roll of honor is called his name should have distinguished mention. Occasionally, when listening to some enthusiast born in a later period, but not in a more modest one, proclaiming as if it were a newfound truth the far-reaching influence of undetected and uncorrected eye-strain and the technique of the determination of the errors of refraction, he would say, with a characteristic quizzical smile, 'If our young friend were as familiar with the literature of his profession as he thinks he is with its practice, he would be saved from the severe effort of rediscovery.'

"In 1880 the officers of the Pennsylvania Railroad invited Dr. Thomson to give advice and assistance to them in their examination of the employés as to sight, color sense, and hearing. He recognized at once the need of a system which, to use his own words, 'could be applied locally on each division, quietly, and at the convenience of the men, without compelling them to lose much time.' This led to his invention of an instrument for the examination of the color sense which is known as 'Thomson's color stick,' with which, while Holmgren's method of matching colored worsteds was adhered to, the examination was simplified, and with

[1] Transactions of the American Ophthalmological Society, 1874, p. 133; ibid., 1875, p. 310.

it records could be made by any intelligent layman from which an absent division superintendent or expert could quickly decide the exact color sense of the man who had been examined. Subsequently Dr. Thomson devised a lamp or lantern as an adjunct to the color wool stick, which served an exceedingly useful purpose, not only in the detection of color blindness, but in eliminating many of the objections which surrounded the wool test. Dr. Thomson's system was soon adopted by other railroads in this country, and his tests have been employed by some railroads in England. In 1896, when Dr. Thomson wrote his most important article on "The Detection of Color Blindness,"[1] he was able to say: 'The total number of corporations which have adopted this system and have used the "color stick" and the new wool test for the detection of color defects is estimated at seventy-eight, having under control a total mileage of 106,395 miles.' Four years later, referring to the same subject, he wrote: 'The system of the Pennsylvania Railroad has been in use since 1881, and has been adopted by other corporations controlling 150,000 miles of track.'[2] Is it not a noble record – the system devised by one man safeguarding the lives of the thousands who by day and by night travel over these many, many miles?

"Two institutions in this city are especially indebted to the work of William Thomson, namely, Wills Eye Hospital, with which institution he became connected in 1868, and in which he served for many years with brilliant distinction, and the Jefferson Medical College, with which school he was identified from 1873 until his resignation in 1897, first as lecturer on diseases of the eye, later as honorary professor of ophthalmology, and finally, in 1895, as full professor of ophthalmology, with a seat in the Faculty. On his resignation, in 1897, the title of emeritus professor of ophthalmology was conferred on him by the Trustees.

"During this quarter of a century he taught with great ability, and was a chief among those who raised ophthalmology to the high plane which it has always occupied in this city. To the development of the daily clinic, which began in 1873, he lent his best

[1] System of Diseases of the Eye, edited by Norris and Oliver, 1897, vol. ii, p. 339.
[2] Transactions of the American Ophthalmological Society, 1900, p. 192.

efforts, working with an enthusiasm which those who assisted him soon caught, until the eye clinic of the Jefferson Medical College became, as it has remained ever since, one of the most important factors in the spread of ophthalmic knowledge and one of the most commendable charities of Philadelphia.

"Those who had the honor to listen to Dr. Thomson's lectures and to follow him in the wards and clinics can best appreciate how admirable a teacher he was. His intimate knowledge of the sciences of ophthalmology gave him an ability to expound its problems to those who came for advice and instruction beyond that which is possessed by most men. He had an enduring respect for his material, and his work left his hands finished with a master's touch. He believed it to be his duty to make clear to patient and to student his conception of the needs of each, and each in turn left his presence with his needs supplied.

"While Dr. Thomson's contributions to the literature of ophthalmology were not numerous, considering the long life he led and the prominent position which he occupied in the ophthalmic world, they were always valuable, always carefully prepared, always instructive, and frequently original. Never willing to place himself on record until he was master of the subject about which he was to write, he naturally wrote with the same clearness with which he spoke and taught. A pioneer in American ophthalmology, he lived to watch its splendid development, lived to see the rise in the value of his own investigations and achievements, lived to receive the high appreciation of those he had taught and whose footsteps he had turned into pathways marked by his own wise directions."

I have so far said nothing of the characteristics which made Dr. Thomson a delightful social comrade and a friend to trust. A certain enjoyment of life and broad intellectual sympathies made him always interesting and always interested. He had learned the fortunate wisdom of multiplied tastes, and while enjoying music with large knowledge, loved all the arts, and was ready with brush and pencil. I have shot with him, fished with him, and once rode with him quite a thousand miles. He was a good shot, a joyous companion at the camp fire, and none of the annoyances of the rough life we led ever lessened his gay amiability; while on a

journey not free from daily peril, he always was of those to whom danger brings calmness, and for whom emergencies increase readiness. As life wore on and the changes brought by time impaired his physical capacity, he adapted himself to changing conditions, resolute to find some new form of exercise. When field sports failed him, at sixty-four he took to the bicycle, and later to golf, which he gave up only when his heart began to deny him the activities of outdoor life.

My friendship for this attractive gentleman, begun in our early days and strengthened as life ran on, without ever a shadow of difference, and with the constant conviction that in every relation of the term "friend," he could be surely trusted to do the kindest and most serviceable thing.

He was a member of the Philosophical Society, the Academy of Natural Sciences, honorary member of the New York Neurological Society, surgeon to the Pennsylvania Railroad, sometime physician to the Episcopal Hospital, and a member of the Loyal Legion. What were his quietly given services to this College you very well know.

LIST OF PUBLICATIONS.

Author of the chapter on Diseases of the Eye in the fifth edition of the System of Surgery of Professor Gross.

Test for Diagnosis of Ametropia with Instrument, 1872.

Ophthalmoscope in Diagnosis of Intracranial Lesions, Mitchell and Thomson, 1873.

History of the First Tumor of Brain Diagnosticated by its Use in Philadelphia.

Astigmatism as a Cause for Persistent Headaches Treated by Correction of Optical Defects, Mitchell and Thomson.

Connection between Posterior Staphyloma and Astigmatism, 1875.

Correction of Conical Cornea by Convex Cylindrical Glasses.

Rapid Diagnosis of Refraction with New Instrument, 1878.

System Adopted by the Pennsylvania Railroad in 1880 for Examination of Employés for Color-blindness, Vision, and Hearing, with Instruments, Color-stick, etc. (still in use and adopted by other roads controlling over 150,000 miles of track).

Supplement to Nettleship on Diseases of the Eye.

Edited the ophthalmic part of the Annual of Medical Sciences in its first year,1889.

New Wool Test for Detecting Color-blindness, 1894.

Chapter on Diseases of the Eye in American Text-book of Surgery, 1892.

Normal Color-sense and Detection of Color-blindness in Norris and Oliver's System of Diseases of the Eye.

Relation of Ophthalmology to Practical Medicine.

Detection of Color-blindness with the Lantern, 1901.

Use of Circles of Diffusion for Correcting Ametropia with an Instrument, with Dr. A. G. Thomson.

There are eight new instruments devised by him that have been accepted as useful by the profession.

This list comprises his principal publications, but there are many clinical reports of cases to the medical journals.

MEMOIR OF CHARLES STEWART WURTS, M.D.[1]

Born April 18, 1830. Died August 14, 1907.

By ROBERT N. WILLSON, M.D.

Those who knew Charles Stewart Wurts loved him as one of Nature's gentlemen. As erect in character as in carriage, there was more in the man than integrity. He was more than law abiding. He had, indeed,

> "A fine sense of right
> And truth's directness meeting each occasion
> Straight as a line of light."

But there was behind the inflexible determination to do no wrong a winsomeness, a kindly something that drew men to him, and a warm heart that won for him many a loyal friend. Providence furnishes us with comparatively few men of real nobility of purpose. Least of all does this genus flourish among the so-called well-to-do. He was born of and among gentle folk, in what was then the newer Philadelphia, on Spruce between Sixth and Seventh Streets. His father gave him for his heritage a record of high religious ideals, well lived up to; and, himself an elder in a strong Presbyterian congregation, bred in the boy that love for a republican representation in church and every other government that found full expression in the life that was to speak so openly for fair dealing and for the observance of the rights of mankind. Even the snow-haired sexton of the church in which he lived and labored for a lifetime loves the memory of the boy whom he remembers seeing, first of all in a blue cap, as he came into the meeting house in company with a stately father. Only one other have I known in recent

[1] Read March 3, 1909.

times of the same cast and mould. Strangely enough, in intimate friendship from boyhood days, grew side by side Charles Stewart Wurts and Henry N. Paul, than whom never lived more quiet men, nor of greater depth; than whom never strove for the good of their fellows men more unselfish and devoted. An old friend remembers them both with warm pleasure as "bouncing boys, close partners in turning-lathe, boat, and toys." Those of us who knew them later in life saw from another bend in the stream the beauty of the clear, deep current, that ran swift and full until it merged into eternity's wide ocean.

Dr. Wurts found little interest in himself as a topic of conversation. As a consequence, neither his family nor his friends have within their possession more than an outline of his early medical life. He was graduated from Jefferson Medical College in 1854, in the sunshine of perhaps as brilliant a medical society as America will ever see. In the faculty that guided his studies were found John K. Mitchell, Dunglison, Pancoast, Bache, Mütter, Huston, and Charles D. Meigs. Two city blocks away there presided over the Medical Department of the University of Pennsylvania another army of giants —among whom were Chapman, Gibson, Jackson, Gerhard, George B. Wood, Hodge, Horner, and his assistant, Joseph Leidy. In such a soil he had every opportunity for rapid culture and growth in his chosen sphere, had not home demands compelled his attention and forced him to withdraw his sign plate from the window almost before it had begun to show the tarnish of weather and time.

His student medical days were spent in the then new building at Tenth and Sansom Streets, into which during his first year several rooms were opened from an adjoining building to form the beginning of the Jefferson Hospital. Fifteen beds were made to supply the clinical needs of a medical institution comprising two classes, each of over two hundred men. A large majority of his classmates were the sons of Southern gentlemen—only 51 from a total of 217 claiming Pennsylvania as their commonwealth. His preceptor during his medical course was the elder Gross, and though little is known of his studies in general, I have heard Dr. Wurts more

than once comment on his association with his friend Da Costa in their joint student and postgraduate work under the master-surgeon. Da Costa preceded him by two years, and was graduating just as young Wurts was entering upon his medical studies; but there was always afterward an intimacy between the two. I cannot refrain from an incident that was told with a relish in my hearing on more than one occasion. On the day the two young men first met, Wurts, on offering his hand to Da Costa in prophecy of and as a seal to their future intimacy, felt the forefinger of the latter slip over to his new acquaintance' radial artery. "Keep still, just a moment, my friend," Da Costa said, "I am studying your pulse." The slight monotony of voice, the deliberate expression, the odd sign of promise in the use of his wrist for clinical study, all amused and delighted Dr. Wurts, and his eyes twinkled with old recollections as he put his own finger on his pulse to recall the touch of the friend who had gone on a little before.

Following his student days at Jefferson, he spent two happy and memorable years in Paris, walking the hospital wards and absorbing the lectures of Louis, Charcot, Andral, Velpeau, Nélaton, Cruveilhier, and Duchenne. Magendie died while he was in Paris. It is not generally known that Dr. Wurts' zeal for scientific study almost cost him dear at this time. According to his own recital, he was in his room in Paris on a very cold night, and had lighted the charcoal brazier, but neglected to provide ventilation and an exit for the charcoal fumes. He recollected afterward simply that there came to his mind an appointment which he had promised to keep, and that rising in a daze he fell against the door, which opened with his weight into the fresh air. On completely reviving, he realized how narrow had been his escape and how much he owed to his habit of keeping appointments, and to his uneasy conscience with regard to this particular one.

I have here tonight one of two volumes on anatomy purchased by him in October, 1854, in the Rue de l'École de Médecine for 104 francs (or $21.00), and the bill for the same. There seems to be no doubt that he was absorbed in earnest preparation for the practice of his profession, and there need be no hesitation in the belief that

success and eminence would have been realized. And yet though a a sign was soon hung from his window ledge to the effect that he was ready to receive patients, and although he had already connected himself officially with the Children's Hospital, Providence had looked farther ahead than he, and after four short years the death of his father and the invalidism of his mother made it necessary for him to devote his immediate entire attention to the interests of the home. As a consequence, medicine lost a natural-born physician, and the world's market was the gainer for a dealer in honesty, uprightness, and honor.

Dr. Wurts was married in 1857, but lost his wife by death within a short time. He was again married in 1865, and became the head of a thoroughly happy home. Few men centre their interests more completely in their children. In the summer of 1883 his wife died, and the home again required of him both a mother's and father's affection and care. He was gradually drawn into business connections, and became the vice-president and a director of the Cambria Iron Works. His duties in connection with these offices proved so irksome and confining that he finally relinquished them, and again threw back his shoulders in perfect freedom.

Two outside interests formed intimate and welcome associations in his life. The first was Calvary Church, in which as a boy I first knew and admired the trim, soldierly figure, and in which I first learned to welcome the warm grasp of his hand. Like his father, the people would have made him an elder in their church government. Preferring, however, to remain under cover in a less conspicuous activity, he declined the honor, and continued until his death to serve as a private in the ranks. Because of his refusal to become prominent in the immediate church government he was none the less active in her service, and was for years not only a member of the Board of Trustees, but the superintendent of her Sunday School.

A second interest that led him to devote a more than occasional evening to serving his fellow men was the College of Physicians. For many years he was its treasurer (1877 to 1893), and long after he was incapacitated for duty his heart was here.

Even in his last years the frequent first inquiry when the members of the family had retired from the supper table was, "What is there new at the College?" Each item was grasped with affectionate interest, seemingly with the longing that he might again share the deliberations of the Fellows, as well as their sorrows and their joys. His friendships among them constituted the one hearty, ever-binding link and reconciling force between a past that had been dedicated to the science of medicine and its relinquishment for cause. Happy memories mellowed impatience into a gentle resignation even to advancing years and to a relentless disability.

It is pleasant to remember that nearly all that was purely medical in his life was closely associated with this College. In his graduation year (1851) the College of Physicians removed to the so-called Picture House, belonging to the Pennsylvaina Hospital, named thus because it contained Benjamin West's painting of "Christ Healing the Sick."

This year also marked a revival in an almost dead interest in the College. The building fund began to grow apace, until in 1863 the College entered the structure which in turn is about to be deserted because outgrown. During the year that opened to his return from study in Paris the Müttur Museum was established and endowed by the Professor of Surgery of his student days. In 1860 the library numbered fewer than 2000 volumes; from that year it entered upon a phenomenal development and growth.

In 1860 Dr. Wurts was elected a Fellow of the College, and in 1877 succeeded Dr. Rodman Paul as its treasurer.

No more need be said of his service than that it rang true, as did all that entered into and came from the life of this genuine man. In our humanly narrow judgment it would seem almost a matter for regret that he was drawn, even by force of unavoidable circumstances, to abandon the task to which his hand had been so devotedly laid. How his sympathy and tact and gentle courtesy would have furthered the perpetuation of the old-time family physician, of whom we have so few worthy examples remaining, whose personality is so fast fading into memory!

Rather let us lay him away for a little time without regret, even

with joy and satisfaction that the fragrance of his friendship has been shared by two worlds—that business and home world that now and again cries out in anguish for the healing touch of some kindly hand, and also this little circle of followers of the same star that attracted him until duty called him another way. We are all broader men for having known and loved him. Some of us wonder that we did not better understand his silent influence when here.

"Soft scentless, feathery flowers of blue
Were in my garden border set;
Beside them, clothed in tender green,
Grew the dear, fragrant mignonette.

"I plucked a spray of blossoms blue,
And kept them with me in my room,
And suddenly I 'came aware
Of faintest fragrance from their bloom!

"I could not think what it might mean,
That such a fragrance I could get
From scentless flowers, until I thought—
They grew beside the mignonette!"

MEMOIR OF HORACE Y. EVANS, A.M., M.D.

By WILLIAM M. WELCH, M.D.[1]

The death of Dr. Horace Y. Evans removes a man highly esteemed, professionally and socially, by all who knew him. In no medical body was his worth better known or more highly appreciated than in this College, of which he was a worthy Fellow for forty years. And nowhere else outside of his immediate family circle is his loss more keenly felt.

Dr. Evans was elected a Fellow of the College of Physicians in 1868. His sound judgment and manly personality, together with the loyal and practical interest which he always manifested in the affairs of the College, justly entitled him to the good-will and esteem of all its Fellows. As evidence of the high estimation in which he was held, and of the confidence imposed in him, I would mention that he was elected by the Council, October 29, 1895, a Trustee of the William F. Jenks Memorial Fund. He was elected as a councillor and served a term of three years—from January, 1898, to January, 1901. In 1902 the College elected him to the responsible office of censor, which office he worthily and faithfully filled until the date of his death. I may add that he was not only faithful in the performance of every official duty which he accepted, but also always was ready and willing to assume the responsibility of his action. Indeed, next to his church, he gave to this College his most earnest, conscientious, and willing service, and has left it the legacy of a good example which each Fellow would do well to imitate or emulate.

I might remark, parenthetically, that the subject of this Memoir

[1] Read October 6, 1909.

was a close and warm friend of the late Dr. John Ashhurst, who was a distinguished and honored Fellow of the College. It is said that Dr. Evans was one of the very few of Dr. Ashhurst's extensive acquaintance whom the cultured and dignified Ashhurst would allow to address him in ordinary conversation by his Christian name, John.

Dr. Horace Young Evans was born in Chester County, Pa. He was of Welsh descent. His great-grandfather, Abner Evans, came to America from Carnavonshire, Wales, in 1717. He landed at Chester, on the Delaware River, and subsequently took out a patent to a certain portion of land in the northern part of Chester County, and named the District "Nantmeal," which title it still retains, and the homestead is yet in possession of his descendants. This particular locality is also known by the name of "Abner's Hill."

Following down the line of Dr. Evans' ancestry, his grandfather's name was Owen Evans, and his father's name, Jesse Evans. Abner, his great-grandfather, married a daughter of the Hon. Dunwoody, a former Governor of Virginia. All of Dr. Evans' ancestors were stern, God-fearing people, and were important factors in giving to the district in which they first settled that high moral tone for which it has since been known.

His grandfather, Owen Evans, must have been a man of considerable prominence and force of character, and noted particularly for executive talent, for while he was not a physician, as I believe, but a tiller of land, he is said to have held the position of Medical Purveyor in the Continental Army during the Revolutionary War.

The writer has been able to learn but little of the maternal ancestors of Dr. Evans. It is known, however, that his mother's maiden name was Mary Young, a daughter of John Young, of Berlin, Pa. Consequently, part of his own name was inherited, so to speak, from his maternal ancestors. His father died in 1872, and his mother's demise occurred in 1881.

Horace Young Evans was, as we have seen, the son of Jesse and Mary (Young) Evans, and was born October 14, 1834. His early education was received at the West Chester Academy, from

which he entered as a freshman at Princeton College in 1851, and was graduated in 1855, with high honors. He was a diligent and painstaking student, and always obtained high averages. As he was in the habit of signing himself H. Y. Evans, his fellow students gave him the name of "Hy Evans," the name by which he was known in college during his student days.

At Princeton, young Evans was a member of the Cliosophic Society and of the Chi Psi Greek Letter Fraternity. During his senior year in college he was honored by being chosen as editor of the "Nassau Literary Magazine," a publication at that time of no mean repute.

As a mark of distinction our Fellow received from Princeton, in 1858, three years after his graduation, the degree of Master of Arts.

He matriculated in the Medical Department of the University of Pennsylvania in the fall of 1855, having as his preceptors Professor Joseph Carson and Dr. Horace Evans, a relative with whom he resided for a number of years, and for whom he held a fond affection, which there is every reason to believe was reciprocal.

With the advancement of medical education and the additional requirements of medical colleges the time of the student is now so completely occupied with college work that the erstwhile preceptor has been entirely eliminated, which, from some points of view, is to be regretted. Undoubtedly much may be learned from a wise preceptor that tends to develop the personal side of the physician's art. Dr. Evans always revered the memory of his faithful preceptors, for from them he learned, both by precept and example, the proper relation between the physician and his professional brethren, the careful observance of the time-honored principles of professional etiquette, and the sacred duty of the physician to his patient and to the community at large. This line of conduct was so thoroughly inculcated in his mind upon entering the threshold of medicine that he held on to it with an unswerving steadfastness throughout his whole professional life.

At the time our deceased Fellow entered the University of Pennsylvania, the medical student was eligible for graduation

upon completing two courses of lectures. He, however, preferred to take three courses, and was graduated in March, 1858. The subject of his thesis was "The Operations for Cataract."

It may be of sufficient interest to mention that the number of matriculates at the session of 1857 and 1858 was 435, and that 143 of these graduated in the class of 1858. In the list of members of this class, along with Dr. Evans, there are also included the names of such worthy Fellows of this College as Dr. George C. Harlan,[1] and the late Drs. James H. Hutchinson and H. Lenox Hodge.

After receiving the degree of M.D., our departed Fellow did not at once locate for general practice, but spent part of his time, in 1858, in certain dispensaries of the city, and in 1859 he went abroad for the purpose of continuing his studies in l'École de Médecine de Paris, and at Guy's Hospital, London, where he received instruction from some of the most noted teachers in the science of medicine at that time.

It should be stated that this was not his only visit abroad. Indeed, he was very fond of travel and observation, and valued highly the benefits to be derived therefrom. His subsequent visits to Europe occurred in 1868, 1897, 1899, 1902, and 1905. These visits were all made while he was engaged in a busy and exacting family practice.

Soon after he returned home from Europe in 1859, he was appointed an Interne at the Episcopal Hospital, and subsequently was elected a member of the visiting staff. At the close of the Civil War he was transferred to the military ward of that Hospital.

Upon the breaking out of the war, Dr. Evans was elected surgeon to the First Troop, Philadelphia City Cavalry, succeeding Dr. Paul Beck Goddard. He entered the U. S. Military Service with his company in 1861. After serving in this capacity for some months—perhaps a year—he resigned and was appointed an Acting Assistant Surgeon of the U. S. Army, and was assigned to duty at the Mower U. S. Army Hospital, Chestnut Hill. He

[1] This memoir was written before Dr. Harlan met with the sad accident which resulted in his death.

continued in the service until the fall of Richmond. While a medical officer at the Chestnut Hill Hospital, he was chosen to serve upon the Board of Medical Examiners, whose duty it was to examine all soldiers in the hospital making application for discharge from military service on account of disability.

After a period of service of five years in various dispensaries and hospitals, both in this country and abroad, and in the U. S. Army, Dr. Evans entered into private practice in this city. He first hung out his sign at the home of his relative, Dr. Horace Evans, 635 Walnut Street. A little later, he occupied, for a short time, an office on Mt. Vernon Street, near Seventeenth Street.

In 1863 he married Anna L. Richards, daughter of Wm. H. Richards, of Philadelphia. His wife died in 1881. In 1885 he was married again. The name of his second wife was Mrs. Ida Martin Williams, a widow, who survives him.

In the year 1865 he purchased the property at the northeast corner of Green and Seventeenth Streets, where he continued to reside until he was removed by death.

The unusual advantages which Dr. Evans had enjoyed since his graduation from the University of Pennsylvania eminently qualified him to commence the work of a general practitioner of medicine, and it was not long until he succeeded in building up a large and lucrative practice, chiefly among the better class of citizens in his neighborhood. His ability, together with honesty and fair dealing, secured at once the confidence of his patients, and this he had to a remarkable degree. He was distinctively a family physician. His mind was fully imbued with the greatness of his mission, and he always endeavored to fulfil, as best he could, the responsibility incurred in accepting the charge of a patient. His skill, attention, and fidelity were so plainly evident as to inspire the minds of his patients with gratitude and respect, as well as confidence. In giving advice to his patients, he was always positive and firm, while his general deportment was characterized by sympathy and tenderness.

Our Fellow never lowered the dignity of his calling by undervaluing his professional services. He always maintained that

the maximum fees charged by the family physician in this city were not too large, and he deemed it a point of honor to adhere to a reasonably high rate of charges for his services with as much uniformity as varying circumstances would admit. In this he was in no sense actuated by a sordid mercenary motive; he was simply upholding the dignity and honor of his profession. For the poor he had much sympathy; and he was ever ready to recognize the valid claims of poverty for gratuitous services.

In professional intercourse with his brother-practitioners our departed Fellow always observed the most honorable and scrupulous regard for what was right and just. Indeed, his sense of honor was so high that it may be said of him that he was even punctilious in his observance of the numerous points of medical ethics and professional etiquette.

Immediately after the close of the Civil War—in 1865—Dr. Evans was appointed Surgeon to the Philadelphia and Reading Railway Company, and served in that capacity for twenty years. He was also for a time physician to an Almshouse District.

Eleemosynary professional services were liberally dispensed by him. For thirty years he served as physician to the Welsh Society of this city; he was a visiting physician to the Charity Hospital for thirty years, and subsequently, until his death, a member of its Board of Directors. He was president of its Board of Trustees, and at the request of the Medical Staff was appointed the first Medical Director of the Hospital.

Besides these appointments, in his earlier professional life he was physician to the Moyamensing House of Industry, the Foster Home, the Northern Home for Friendless Children, and the Industrial Home for Girls.

Dr. Evans was a member of a large number of medical organizations, among which may be mentioned, besides the College of Physicians, the Philadelphia County Medical Society, the Medical Society of the State of Pennsylvania, the American Medical Association, and the American Academy of Medicine. For twenty-five years he was a member of the Sydenham Medical Coterie, an organization whose origin dates back nearly half a century,

and whose membership is limited to twelve. Upon presenting his resignation to this coterie he was unanimously elected an honorary member, a mark of respect that has been shown to none other.

He was elected to membership in the Philadelphia County Medical Society in 1864, and during his connection therewith took an active part in all of its affairs. In 1866–67 he was assistant secretary of the Society, and for the three subsequent years its corresponding secretary. He was elected a censor in 1871, and served in that capacity for about ten years. In 1881 he filled the position of first vice-president of the Society, and in 1882 was elected its president.

Dr. Evans held very positive views in opposition to a mixed audience of male and female practitioners of medicine at clinics, in teaching, and at meetings where certain medical subjects were discussed. His sense of propriety was so nicely determined that he felt that such procedures would prove demoralizing and debasing to both sexes. In his retiring address as president of the Philadelphia County Medical Society, he spoke as follows:

"Mr. President, there are gentlemen in this Society who conscientiously believe that mixed clinics, mixed classes in teaching, and mixed audiences at lectures on certain subjects in medicine are demoralizing, debasing, and disgraceful.

"And, sir, I envy not the man who can stand upon this floor and indiscriminately support either. The presence of women at our meetings will so outrage the sense of delicacy and propriety of some of us that we will be forced to withdraw therefrom.

"I therefore appeal to every friend of the Society to exercise his personal influence in every honorable way to banish this ferment which has already so soured our feelings."

After many years of constant and heated discussion, threatening at times the harmony and usefulness of the Society, the question of admission of women physicians to membership was finally settled in 1888, when a female candidate secured the necessary two-thirds vote, and was declared elected. True to his convictions, Dr. Evans at once severed his connection with the Society

by promptly forwarding his resignation. Immediately he transferred his activities in matters medical from that Society to this College.

Our departed Fellow was not a prolific writer. His productions, however, in the field of medicine were all of a markedly practical character and based upon his personal experience. So far as I know, the following is a complete list of extant publications from his pen:

In 1866, he contributed to the *American Journal of the Medical Sciences* a paper on "Poisoning by Stramonium;" in 1867, another on "Potassium Bromide," and in 1875, one on "Pruritus Formicans." He published in the *Medical Times and Medical News* papers on "Chloral," "Pertussis," "Phthisis," "Hypodermic Use of Morphine," "Strapping in Pulmonary Disease," "The Pulse and its Indications," "Literature of Enemata," "The Distant Action of Glycerin Suppositories," "Poisoning from Fungi," and "Conjugal Diabetes." To the archives of obstetrics he contributed a paper on "Deformities in the Fetus following Accidental Hemorrhage during Pregnancy."

Dr. Evans was one of the original managers of the University Hospital, and continued to serve upon the Board of Managers for twenty-four years. He was secretary of the Board of Contributors to the Hospital Fund from its organization. He was one of the originators of the Medical Alumni Association of the University of Pennsylvania, and took an active part in this organization as long as he lived.

He was vice-president of the Welsh Society of this city, as well as its medical adviser; and he was a comrade of the Grand Army of the Republic. In politics he was a staunch Republican, but never held any political office.

Dr. Evans was a devout Christian. He joined the Episcopal Church at quite an early period of his life, and was always a regular attendant upon the religious services of his church. For forty years he was a vestryman, and subsequently the rector's warden. He found time in the midst of a busy practice to teach a class in the Sunday school, and he did this with the highest

sense of devotion to duty in the service of his Master. He was no mere theoretical, but a practical Christian. In the daily walks of life he endeavored to live up to the religious principles which he had avowed. Without being in any sense obtrusive, he yet quite unconsciously exemplified in intercourse with his fellowmen the divine injunction: "Let your light so shine before men that they may see your good works, and glorify your Father which is in Heaven."

Apart from his Christian life, Dr. Evans possessed many striking characteristics as a man. He was positive. He was affirmative. He was courageous. He believed in honorable and fair dealing. Perhaps his chief characteristics were simplicity and directness of thought, sturdy honesty, courage of his convictions, and plainness of speech, amounting at times almost to brusqueness. He possessed the capacity for just and impartial action regardless of consequences. He applied to himself this very apt quotation: "With warmth gave sentences, yet was always just." His criticism of a wrong act was often very severe, and he felt that due punishment should follow; but his high sense of justice was tempered with kindness and mercy. One could not associate with him very long without feeling the influence of his dignity and fairness, and especially the example of his correct and honorable life.

Physically considered, our departed Fellow was not vigorous—his stature and weight being somewhat under the average. Yet his fund of vitality was remarkable. He was but seldom incapacitated for work by illness. He was, however, noted for his energy and perseverance, and these qualities doubtless prevented him from yielding readily to physical infirmities. Many years ago he developed pneumonia, and suffered a relapse, but fully recovered.

The month of July, 1908, was extremely warm in Philadelphia, and while attending to his professional work he was apparently overcome by the heat. Believing that he would be benefited by removal to a cooler climate, he decided to go to the coast of Maine. After a long and wearisome journey, he arrived at the

Hotel SamOset, Rockland Breakwater, Me., July 9, greatly exhausted. His illness very soon assumed a serious nature, and death occurred July 23, from apoplexy. His body was brought home and interment took place July 27, in West Laurel Hill Cemetery.

It may be said of Dr. Evans that he died, as it were, in the harness of his profession after an honorable service in his chosen work, which he loved so much, extending over a period of fifty years and four months. Browning has said: "Dear Work! Art thou the curse of God? What must His blessing be?"

As a shock of corn fully ripe for the harvest, Dr. Evans was, by the great Husbandman, gathered home in the seventy-fourth year of his age. A widow and a son—Horace Y. Evans, Jr.—born of his first wife, survive him.

Upon learning of his death, the Board of Trustees of the Charity Hospital placed on record the following minute:

"*Whereas*, It has pleased Almighty God to take from this life our well-beloved co-worker and fellow trustee, Horace Y. Evans, M.D.

"*And whereas*, By his death the Charity Hospital has lost one of its most valued advisers, who for upward of forty years has given to it as a member of its Board of Trustees unstintedly of his time and thought—having served on its Medical Staff, as the president of the Board of Trustees and, at the unanimous request of the Medical Staff of the Hospital, as its first medical director.

"*And whereas*, Dr. Evans, by reason of his unfailing kindness and courtesy, and his very high sense of honor, made himself, unconsciously, an exemplar of moral rectitude, and well-beloved of those who had the privilege of his friendship.

"*Therefore, be it resolved*, That we hereby express our grief caused by the loss of our friend, and record our appreciation of his services, to which the present success of the institution is admittedly so largely due, and testify to the sincere love and affection had for him by everyone honored by his friendship."

At a meeting of the Sydenham Medical Coterie the following notice of his death was read by Dr. Walk, and ordered to be inscribed on a page in the Minute Book:

"Our departed comrade, Dr. Evans, deserves a threefold encomium. He was an honorable gentleman, an able physician, and a sincere Christian. He had three great blessings, a trio of Providential favors not given to many: (1) He seems to have wholly escaped the unbelief now so prevalent among physicians, and to have had a firm faith quite unshaken by the attacks of agnosticism. (2) He was spared the disability which overtakes many men before they reach the age that he attained, and he was able to pursue the work he loved up to the last month of his earthly life. (3) He was not called to bear the bitter trial of a lonely and desolate old age, for he had around him loyal and sympathetic friends, and in his last hours he was attended by those who loved him."

THE ANNUAL ADDRESS OF THE PRESIDENT.[1]

By JAMES TYSON, M.D., LL.D.

Since the reading of my last annual address, January 1, 1908, the interest of the Fellows of the College has been largely centred on the progress of the new hall on Twenty-second Street. That it is quite deserving such interest and attention must be evident when it is recalled that the College has thus far appropriated toward the cost of construction and furnishing the building $295,000. Such an undertaking has never been assumed by a medical society in this country or perhaps anywhere. The building of the Royal College of Physicians in London approaches it most nearly. Much thought has been spent on the elaboration of the plans by the Building Committee in conjunction with the architects so as to adapt them to the various purposes of the building as a library, a resort for students, authors, and investigators, and a meeting place for societies. I hope I will not be regarded as suggesting a misuse when I say this new home may also serve somewhat the purposes of a club house, where our Fellows can meet and discuss appropriate subjects. Even to *lounge* in an atmosphere of books is uplifting, and more than once has stimulated literary thought and literary research. The progress of the building has been as satisfactory as could be desired. Ground was broken on January 30, 1908, and the cornerstone was laid April 29, with simple but appropriate ceremonies, consisting in prayer by Bishop Whitaker and short addresses by the President and Dr. S. Weir Mitchell, who laid the cornerstone. As the building rises, a clearer conception of its size and proportions can be obtained. It is a typical example of

[1] Read January 6, 1909.

the Georgian period, dignified, impressive, and quite in keeping with the age and traditions of the College. There is every reason to believe it will be completed and ready to hand over to the College by the contractors on or soon after the date agreed upon, May 1, 1909. The increased running expense which must naturally follow the occupation of this larger and more luxurious abode has necessitated an increase in the annual dues and initiation fee, which has been provided for by a recent action of the College, and I think the Fellows will quickly recognize that they are receiving a corresponding equivalent.

The papers read before the College during the year have been more numerous and more extensive than in 1907, and a correspondingly larger volume of TRANSACTIONS will be the result. Still larger and more valuable would it be if the papers read before the Sections could be included, the absence of sufficient funds necessitating their omission. I cannot but feel that such omission is partially responsible for what I may call "the decline of the Sections," three having been entirely discontinued, while that on Medicine, the most important of all, has reduced its meetings to two for this year. When men take the trouble to prepare papers, they reasonably expect their publication to be provided for.

This seeming decline has been a great disappointment to me, for I have heretofore looked forward to the day when the nine monthly meetings in the year would be devoted to necessary business and papers of general interest to physicians, surgeons, and specialists alike, while the papers on special subjects would be read before appropriate Sections. With the laying down of the Sections it would seem that this hoped-for day is not likely to be soon realized.

That such a plan is in accord with modern tendency is shown by the recent formation in London of "The Royal Society of Medicine," by the consolidation of sixteen societies, including the Royal Medical and Chirurgical Society, the Pathological Society, the Clinical Society of London, and other influential societies, which become sections of the new society. There is an annual fee of three guineas for each Fellow, with an entrance fee. The society

started with a membership of 3000 and with a library, by union of the special libraries, of 70,000 volumes, making it the most comprehensive library in the United Kingdom.

[4] The provision of a Committee on Scientific Business has proved a success, and I believe it is at least partly due to its efforts that the papers read to us also exhibit an improved quality, as well as that they have been more numerous. Among them may be mentioned those on "Aneurysm," by Drs. Anders, Sailer, McFarland, Steele, Pancoast, and Hare, at the February meeting; that on "Diseases of the Joints," by Dr. Goldthwait, of Boston, at the March meeting; those on the "Lumière Process of Color Photography," by Drs. Schamberg and Hartzell, at the April meeting; that on "Pellagra," by Dr. Edward J. Wood, of Wilmington, North Carolina, at the November meeting; and that on the "Cammidge Reaction in Experimental Pancreatitis," by Drs. Speese and Goodman, at the December meeting.

Our Library must continue to be the object of anxious solicitude as well as of pride. The last annual report of the Library Committee showed the following:

Number of volumes	86,718
Unbound theses and dissertations	22,681
Unbound pamphlets	67,122

In detail as follows:

Number of bound volumes in the Library	77,603
Number of unbound reports and transactions	9,115
Number of unbound theses and dissertations	22,681
Number of unbound pamphlets	67,122

The increase in the use of the Library for the past year was a little more than 40 per cent.—actual increase in the number of visitors, 5110.

Increase in books consulted, 10 per cent.

Increase in books taken out, 10 per cent.

We claim to have the second medical library in the country, for value of its collection and size, ranking next to that of the Surgeon-General's Office. The recent addition of Paris theses (more

than a score of years and nearly a thousand volumes), of foreign exchanges, of incunabula and other rare works, many of which were obtained through the efforts of our esteemed ex-president W. W. Keen, have materially added to the number and value of our books. Dr. Keen's efforts should be imitated by others.

It has been suggested that advantage be taken of the meeting of the American Surgical Association in Philadelphia in June next and of the American Medical Association at Atlantic City to have an exhibition of rare surgical and medical books, instruments, and curios in the Mütter Museum. In like manner advantage might be taken of the dedication of the new Hall for such an exhibit. I invite the attention of the Building Committee and the Entertainment Committee to these suggestions. No opportunity should be lost to influence gifts and endowment to the library.

Death has dealt gently with our Fellows in the past year. During the year ending December 1, we have lost by this cause four Fellows and two Associate Fellows. The former were: Dr. Henry D. Benner, died December 8, 1907; Dr. L. D. Judd, died March 18, 1908; Dr. J. Dutton Steele, died May 17, 1908; Dr. Horace Y. Evans, died July 23, 1908.

Two Associate Fellows died, one American, Dr. Nicholas Senn, January 2, 1908, and one Foreign, Professor Felix Terrier, of Paris, France, April 18, 1908.

Allusion was made to Dr. Benner in my last annual address, under the impression that the year covered January 1, 1907, to January 1, 1908. He became a Fellow in 1860. He was, therefore, one of our oldest fellows.

Dr. Leonardo da Vinci Judd became a Fellow in 1885, and died March 18, 1908. He had a large general practice in West Philadelphia and was highly esteemed by his patients.

Dr. Steele was elected a Fellow in 1898, and died May 17, 1908. Gentle and refined, he was courageous beyond most men in contending against an infirmity which did not prevent him from becoming a scholarly and accomplished physician and research student whose name is permanently placed on the roll of scientific physicians.

Dr. Horace Y. Evans was also one of the older Fellows of the College. He was elected a Fellow in 1868, and died July 23, 1908, after forty years' membership. He was aggressively conservative, had the courage of his opinions, and spoke them. He served the College faithfully for many years as a Counsellor and Censor. He was also one of the few surviving Fellows who served their country in the Medical Corps of the Army during the Civil War, and was for a time a prisoner in Libby Prison in Richmond.

Dr. Nicholas Senn became an Associate Fellow in 1886. Born in the canton of St. Gall, Switzerland, he came to the United States with his parents when he was nine years old, settling in Wisconsin. His education, general and medical, was received in the West, and he soon acquired a world-wide reputation as an author, teacher, surgeon, and traveller. At the time of his death he was Professor of Practical and Clinical Surgery, Rush Medical College, and Professor of Surgery in the Chicago Polyclinic.

Dr. Felix Terrier was chosen a Foreign Associate in 1907, and died in Paris, April 18, 1908. He was an eminent surgeon, a voluminous author, Commander of the Legion of Honor, Member of the Academy of Medicine, and Professor in the Faculty of Medicine of Paris.

The Censors have directed that memoirs should be prepared of Dr. Evans and Dr. Steele.

There was one resignation of Fellowship, and eight, five of whom were non-residents, forfeited their Fellowship. Twenty-seven gentlemen were elected to be Fellows, the net gain being fourteen, as compared with eleven last year.

The roll of the College on December 1, 1908, includes:

Fellows		444
Associate Fellows (American)	21	
Associate Fellows (Foreign)	19	
		40
Corresponding Members		4
		488

The College has carried out my suggestion of last year that the accounts be kept in a more business-like manner, and the new order

of affairs went into effect December 1. As a result, we have a Superintendent of the building who is responsible for its management, its cleanliness, and a courteous treatment of visitors, and a book-keeper who keeps all the accounts of the College except those of the Mütter Museum. The plan has been too short a time in operation to judge of its success, although this seems reasonably assured.

THE RÖNTGEN RAYS AS AN AID IN THE DIAGNOSIS OF CARCINOMA OF THE STOMACH.[1]

By GEORGE E. PFAHLER, M.D.

Since "35 per cent. of all visceral carcinomata are found in the stomach,"[2] and since surgeons believe that if this disease is recognized early many lives can be saved or prolonged, it behooves us to bring to our aid every means that will assist in making the diagnosis.

From time to time new methods have been added, each claiming superiority over the others and giving us a sense of exactness and certainty. As time passes, each new method is found to have so many exceptions or possible errors that we are likely to go to the other extreme and cast each aside as useless, to grasp at something new. This may also be the fate of this latest and, apparently, the most valuable and exact means at our command. I can already see many possible errors, and, unless the work is done thoroughly and most carefully, and performed by an expert, or, at least, by one who is cautious and not too ready to jump at conclusions, it, too, is bound to fall into discredit.

We shall be on safe ground if we look upon this method only as an aid, and combine with it all the information that may be obtained by other methods of investigation.

True, the exploratory operation is probably the final means of exact diagnosis, but who is willing to submit to this method of investigation until all others have been exhausted?

[1] Read January 6, 1909.

[2] Virchow, quoted by Rodman in Surgery, Gynecology, and Obstetrics, June, 1908.

Holzknecht and Jonas[1] have been the most faithful and thorough investigators that have yet made records in this new field of Röntgen diagnosis of carcinoma of the stomach. Their studies followed and were made possible by Rieder's[2] masterful work in the study of the size, shape, movements, and position of the stomach.

Importance of Using both the Plate and the Screen. In the investigation of the stomach for carcinoma, probably the most valuable evidence is obtained upon the fluorescent screen. By it we recognize the moving food, the moving stomach walls, and the constant variations during the process of filling, which are impossible by any other means. On the other hand, the plate will serve to record permanently and accurately the pathological findings at each step, and will demonstrate finer detail than can possibly be seen upon the screen. Therefore, both Röntgenoscopy and Röntgenography should be used in each case. This will, of course, double the time and expense, but no case is thoroughly studied without both methods.

The serious objection to the use of the fluorescent screen is the danger to the operator. Eight men have already sacrificed their lives through this exposure. It is doubtful whether we can eliminate all danger, but certainly all the protection possible should be provided, or fluoroscopy had better be omitted.

Much unnecessary exposure can be eliminated if a thorough clinical study has been made previous to the Röntgen examination. For this reason the Röntgenologist should be given all the clinical data, so that he may concentrate his attention upon the affected region. So often patients and occasionally physicians expect us to look through the patient, as one would look through a window pane, and see all that is on the inside of the integument. For instance, patients are sent because they have pain in the abdomen, with no other clinical data. Then we must hurriedly guess whether the stomach, the gall-bladder, the kidney, the bladder, or the intestines are most likely at fault, and proceed accordingly in

[1] Die Radiologische Diagnostik der Intra- und Extraventrikularen Tomoren, Moritz Perkes, Wien, 1908.

[2] Fortschritte a. d. Gebeite d. Röntgenstrahlen, February 14, 1905.

making our examination. For the technique for each of these organs is different, and we are likely to obscure the one while examining the other.

Data Forming the Basis of this Paper. The data forming the basis of this paper has been obtained from a study of twenty-nine cases in which evidence of carcinoma was clearly demonstrable, and in most of which this diagnosis was confirmed by operation, autopsy, or the subsequent clinical course.

It is true that in most instances the disease was well advanced, and the clinical evidences of carcinoma fairly strong; but in the majority of cases the tumor was not defined or at all palpable, and in all cases it served definitely to locate the disease and more or less indicate its extent.

This work is still in its infancy, and we must collect evidence for the present from all cases; but I feel that later we should be able to make earlier diagnoses, for the evidence shown late should be present to a sufficient degree rather early.

Evidences of Carcinoma. The evidences of carcinoma of the stomach may usually be classed under changes in the course of the food through the stomach, or changes in outline, position, peristaltic movements, or the mobility of the stomach.

1. *Abnormal Course of the Food.* The course of the food is probably best studied by watching the first swallow, and for this part of the examination a tablespoonful of a mixture of bismuth subcarbonate and water had best be used. This is then watched carefully as it passes from the upper to the lower pole. To recognize evidence by this means, one must first be familiar with the normal course of the food and the possible changes in the course due to other conditions than carcinoma. Briefly stated, it curves about two inches to the left of the median line and takes the shape of a funnel in the upper third of the stomach, with the point downward, and a small collection of gas (usually swallowed air) under the dome of the diaphragm. From the point of this funnel it moves downward, usually in a straight or only slightly curved line, to the lower pole, which may be located anywhere between two inches above the umbilicus and the crest of the pubes.

When carcinoma is present between the upper and the lower pole of the stomach, the food is likely to take an irregular course, as if curving around an obstruction, just as the rivulet curves around a rock. This is best seen when the walls are in contact. When the walls are relaxed or widely separated, as in some advanced cases of gastroptosis, the food drops suddenly from the upper to the lower pole as in an open sack.

Here we must avoid errors, for occasionally extraventricular conditions, such as a distended knuckle of intestine or the pressure of a tumor from the outside, may also change the course. These, I believe, can usually be differentiated by various manifestations, depending upon the ingenuity of the examiner in each case.

This first portion of food can then be watched at the lower pole, as the peristaltic waves carry it forward. Then the stomach should be further distended and the course watched. This evidence can, of course, only be obtained upon the screen, and I consider it very valuable.

2. *Gross obstruction to the passage of food* such as is best illustrated in an hour-glass contraction of the stomach. This is usually evidence of advanced disease, though it may at times be found before palpable signs are present, and even before the symptoms are definite.

Such obstruction can be observed upon the screen, and the degree of obstruction can be estimated by finding the smallest sized portion of food that cannot pass. For this purpose I use various sized pills or capsules of bismuth, but these pills should only be used after one has observed the degree of delay to the passage of bismuth and water and then the thicker liquid of bismuth and kefir.

One must be cautious in diagnosticating hour-glass contraction. There is normally a delay of several minutes at the juncture of the upper and the middle third of the stomach. Gross obstruction cannot be diagnosticated, therefore, until the stomach has been fully distended and until an attempt has been made to crowd food by massage and abdominal contraction from the one segment into

the other. Here, again, particularly in the middle of the stomach, a distended colon may produce a marked indentation and by intra-abdominal pressure cause considerable delay to the passage of the food.

3. *Localized or General Diminution of the Stomach Shadow.* This diminution of the stomach shadow is usually localized and will be most often found at the pyloric end. There is, in addition, usually some irregularity in shape. Such diminution may at times only be seen when the stomach is partially filled, or, again, when nearly empty. This can be understood when one considers that if the tumor occupies either the anterior or the posterior wall without affecting the lesser or the greater curvature, the evidence of obstruction or diminution of shadow would only be seen at a certain stage during which the opposite wall is in contact with the tumor. After the stomach is fully distended a sufficient layer of bismuth will overly the tumor and obliterate the differentiation.

When such evidence is first observed, while the stomach is partially filled, an attempt should be made to carry food into the affected area by massage. If this is impossible the evidence becomes stronger.

4. *Abnormal Contour.* Anywhere along the greater or the lesser curvature there may be a tumor. This would ordinarily cause an indentation in the shadow cast by the bismuth contents of the stomach. Such indentation should first be observed upon the screen. It should be constant, and not obliterated by massage or peristaltic action or respiratory movements. It should then be recorded upon the plate, where finer detail and at times the indentations of the growth itself may be observed. In order to make such a fine detailed record, the exposure must be made in a few seconds, usually under five, so as to eliminate the effect of respiratory and peristaltic movement. Such short exposures require powerful currents, and powerful currents burn up tubes very rapidly, thus decidedly increasing the expense.

Caution: We must avoid the error of interpreting an indentation into the gastric shadow as carcinoma where it is only produced by a distended knuckle of intestine. Such indentation is

smooth, and is usually found on the greater curvature at about its middle or upper portion.

So, too, a strong and slowly moving peristaltic wave, if not observed upon the screen and only seen in one plate, may lead to an error. When in doubt, the examination should be repeated.

5. *Interference with the Peristaltic Wave.* Peristaltic waves in general are plainly observed only in the lower third of the stomach, and best when the stomach is only partially filled, or, again, when nearly empty. Their depth and frequency vary considerably in different individuals. They serve as evidence of carcinoma when they are plainly visible, and are seen to stop at a certain point either on the greater or the lesser curvature. The evidence becomes stronger if they can be seen to begin again farther along on the border of the stomach.

6. *Abnormal Position or Immobility of the Stomach.* The stomach may be drawn by adhesions or crowded out of its normal position by the tumor mass. Adhesions may even twist the stomach so as to divide it into two distinct portions and give the effect of an hour-glass contraction. Such effect was observed in a case of Dr. Rodman's, in which it took the bismuth-kefir mixture nearly one-half hour to pass from the upper to the lower segment of the stomach. The stomach itself was a very large one, so that the lower pole extended nearly to the pubes. The carcinoma was found on the lesser curvature, near the pylorus, with adhesions to the liver higher up, which twisted the stomach and divided it near its middle.

Adhesions below or anteriorly will render the stomach less mobile, but one must bear in mind that with large stomachs and relaxed abdominal walls, the mobility is not great. I usually depend upon abdominal contractions to move the stomach, though pressure with the hand may be used. Such evidence is best obtained upon the screen, but some evidence may be obtained by plates, if one takes a posteroanterior view in the erect posture and an anteroposterior view in the supine posture (with the patient lying upon the back).

7. *Abnormal Evacuation.* In two cases I have observed the stomach contents pass directly into the duodenum almost as fast as they entered at the cardia. This I interpreted as being due to a patulous pylorus. I believed that induration of the walls of the stomach prevented the pylorus from contracting and closing the orifice. One of these cases, belonging to Dr. Daland, died in a few months, with all the characteristic symptoms of gastric carcinoma, but there was neither an exploratory operation nor an autopsy.

The other case belonged to Dr. Anders[1] and was operated upon by Dr. Rodman, confirming in every particular the Röntgenological findings.

There may also be great delay in the evacuation of the stomach due to pyloric stenosis. Here, again, we must be cautious, for I have observed in cases of marked gastroptosis, in which there was no pyloric stenosis, retention of food as long as eleven hours. Retention of food can be interpreted as due to carcinoma only when it is combined with other evidence, both clinical and Röntgenological. Generally, the food should be followed through the bowel to detect other possible involvement, due either to malignant disease or adhesions.

I have prepared about seventy-five lantern slides for demonstration. Many of the plates from which these lantern slides were reproduced were made under unfavorable circumstances, such as hot weather, imperfect apparatus, weak and unsteady or uncontrollable patients, and, as a consequence, are not all good. However, I believe each one will demonstrate some fact.

General Technique.—The technique can only be given in a general way, for in the study of a case one step leads to another and good results will often depend upon the ingenuity of the operator.

1. *Position of the Patient.* This will, of course, vary very much with the individual patient, and several positions are often necessary to confirm or to demonstrate more clearly. Generally the standing posture, with the abdomen against the plate or screen, will give the

[1] Pennsylvania State Medical Journal, November, 1908.

most evidence, probably because in this position the stomach is more stretched out, and because we can best watch the passage of the food, which is conveyed downward both by gravity and peristaltic action.

Lying upon the abdomen for postero-anterior view will probably be the next most valuable. Then one can easily, either in the erect or recumbent posture, change to the oblique or posterior views.

2. *The Bismuth Mixture.* At the very beginning of the examination it is usually best to use a tablespoonful of a mixture of bismuth and water. This will give the greatest density with the greatest fluidity, and it can therefore be best followed in a tortuous course, and into crevices; but one must not use too much of this mixture for fear of the water becoming absorbed and leaving the bismuth in hard masses.

For general use and for further distention of the stomach, I have found a mixture of bismuth and kefir (or Yolack), previously described,[1] to be most serviceable, since it keeps the bismuth in almost perfect suspension and is easily digested.

The remainder of the technique, with regard to the management of the tube, the apparatus, the dress of the patient, the patient, and the plates, will be similar to that used in other abdominal examinations.

Conclusions. -1. Gastric carcinoma is demonstrable when it will change the course of the food through the stomach; where it will decrease the volume, interfere with peristaltic action, fix or displace the stomach, cause an indentation in the stomach wall, or modify the rate of evacuation of the gastric contents.

2. I believe that with this aid a diagnosis can be made earlier than has heretofore been possible.

3. As a rule it is a tedious and expensive study, and therefore each case should be studied well first clinically.

4. Great caution and thoroughness will have to be observed or errors will be made, and this valuable method of investigation will fall into discredit.

[1] Journal of the American Medical Association, December 21, 1907.

DISCUSSION.

Dr. James M. Anders: The subject of Dr. Pfahler's paper is one of the utmost practical importance. It is generally conceded that an early positive diagnosis from the standpoint of our modern ideas as to treatment, at all events, is impossible at the present day. Therefore, any new method which facilitates an early recognition of this grave disease must be welcomed indeed. Dr. Pfahler very properly inclines to the view that the *x*-rays are to be regarded as being simply an aid rather than an absolute, or exclusive, means of recognizing the affection. If, however, the position which he assumes, namely, that by the combined use of the fluoroscope and radiograph we are able to recognize gastric carcinoma at an earlier stage than was heretofore possible, a very important step, it seems to me, has been taken in advance.

So far as my observation goes with reference to exploratory operations in early gastric carcinoma, I may say that in all cases the disease was found at operation to be well advanced, too far in the majority of instances to hope for a cure from extirpation. We are, therefore, sadly in need of means and method whereby we can recognize gastric carcinoma in its incipiency. Again, physicians have not as yet learned the important lesson mentioned by Dr. Pfahler, that in sending patients to Röntgenologists, all available clinical data should accompany them, so that the examiner may concentrate his attention not only upon the organ implicated, but upon the region likely to be involved. Not only can the size and position of the stomach be determined by the *x*-ray expert, but also small masses which may, or may not, be due to carcinomatous growths. This he does by noting first any deviations or deflections in the course of the food in its passage through the stomach, any indentation on the margin of the shadow cast by the bismuth mixture due to the presence of a mass. There can also be noted an arrest of the peristaltic wave at the same point. When we have these three points in the same case we have, as a rule, striking confirmation of gastric carcinoma in clinically suspicious cases. I may say that in one of my own suspected cases recently Dr. Pfahler was able to satisfy himself of the presence of a small mass before it could be felt. This, then, must be considered a decided advantage over the older methods of examination. Before we can, however, estimate the precise value of this method, further studies carried on in the thorough manner in which Dr. Pfahler has been working must be made.

Dr. Judson Daland: It is about two and a half years since I began working with Dr. Pfahler with the *x*-rays in connection with gastro-intestinal affections, and in that time much progress has been made. We are all agreed that the *x*-rays are often an exceedingly important aid in recognizing diseases of the alimentary tract. Therefore, being an aid, we can without argument understand how very important they are in diagnoses in this particular region.

In the recognition of esophageal tumors the fluoroscope has been invaluable. It is a most surprising experience, after having looked at the question of esophageal stricture from the ordinary clinical standpoint, to witness the behavior of the esophagus when it is the seat of stricture. The kefir and bismuth first cause marked dilatation, at times sufficient to contain the entire glassful swallowed afterward, slowly passing through the stricture into the stomach. Of course, the *x*-rays do not pretend to give the nature of the obstruction, but it is important because the obstructive signs seen by means of the *x*-rays in conjunction with other factors in the case frequently establish the diagnosis definitely. It is interesting to observe the difference of certain stomachs shown by Dr. Pfahler under varying conditions.

In one of the cases of gastric carcinoma to which he referred we were never able to secure gastric contents by the stomach tube after a test meal. We supposed that there was an hour-glass contraction, and that the tube was thus prevented from engaging the gastric contents which had already passed to the lower hole of the stomach. The fluoroscope showed, however, that all food swallowed passed quickly through the stomach and into the duodenum, so quickly, in fact, that it was difficult to obtain a good plate.

One of the important advances in the *x*-ray of the œsophagus is the technique by which the œsophagus may be seen by looking through the thorax diagonally, then avoiding the shadows of the sternum and vertebral column.

I believe we have in the Röntgen rays an extraordinary and valuable additional aid in the diagnosis of carcinomatous conditions in the alimentary tract.

I have also been impressed with the great value of fluoroscopic studies, particularly in those suspicious cases in which we cannot escape from the thought that perhaps carcinoma is present. In other words, the negative value of the fluoroscope and skiagraph has been in my experience of very great value.

The study by means of the *x*-rays is one that can only be attempted by one continually doing this work. It requires not only a trained eye able to observe the shadows upon which opinions are based, but it also requires acute and trained observation in order to note the various accidental and temporary conditions which may produce shadows exactly resembling those produced by disease such as carcinoma. Errors are very easily committed, and, therefore, it seems to me that this work must ever remain in the hands of the specialist. I have a difficulty in seeing things that can be plainly perceived by Dr. Pfahler, and in some instances I have failed to see things visible to him. Therefore, it is plain that a negative result from the skiagraphic study is of no particular value unless the work is performed by an expert.

In conclusion, I desire to dwell upon the value of fluoroscopic examination, which often gives more information than the skiagraph. The screen shows organs in motion but one phase of which is recorded by the skiagraph.

Dr. Joseph Sailer: I fully agree with what the speakers have already said. I have some time since reached the general conclusion that when carcinoma of the stomach can be diagnosticated by the ordinary clinical means it is too late to operate. Indeed, in my experience it is nearly always too late to operate no matter how strongly operation is advocated. The value of the *x*-rays as an aid is considerable. There was a patient in your ward, Mr. President, in which the *x*-rays were taken and Dr. Pancoast reported an indentation along the greater curvature. The gastric contents were perfectly normal in all respects. Nevertheless, an operation was performed in view of the other symptoms. These were visible peristalsis, which was observed on one occasion, and manifest deterioration in the patient's condition. A scirrhous carcinoma was found on the greater curvature.

The statement that carcinoma at the pylorus is the most favorable for diagnosis by the *x*-rays has not been my experience in the two or three cases I have seen. There is no very obvious evidence on the plate that tumor exists, because these masses are in such position that they are not liable to produce indentation. We merely find dilatation of the stomach. Fortunately, tumors of the pylorus usually produce such distinct disturbance in the motility of the stomach that other indications for operation always exist and the fact that the *x*-rays frequently show only a dilatation which can be readily recognized by other methods renders them of no great importance. The point is, I think, that in all suspected cases of chronic gastritis the *x*-rays should be taken at the earliest possible moment, and if any suspicious feature exists, then an operation should be performed. I am not sure that the ordinary exploratory operation is of much use. I have seen very distinguished pathologists at autopsies upon cases where some thickening existed in the walls of the stomach in doubt until the microscopic sections showed the nature of the pathological process. If this is the case, even though the stomach has been opened, it must be still more the case if the surgeon has merely the external surface of the stomach on which to depend. Of course, if a tumor is found, it may be an easy matter to remove it. On the other hand, in very early stages of carcinoma, when perhaps a very small nodule exists, or slight thickening, there may be no definite indication for the performance of a serious operation, when, as a matter of fact, it is the only time when a serious operation will be of any benefit to the patient.

Dr. Henry K. Pancoast: I may state that the body of Röntgenologists who listened to Dr. Pfahler's report at the recent convention of the American Röntgen Ray Society, in New York, were as much impressed with the valuable work he has done as have been those who have listened to the paper he has just presented. Dr. Pfahler has been more fortunate than many of us in having so large an amount and so great a variety of material at his disposal. When one examines, perhaps hardly more than one case of carcinoma of the

stomach a month, on an average, conditions are not so favorable for comparative study and investigation as is the case when the examiner has a number of patients at his disposal at one time. There is still a great deal to be learned from the *x*-ray examination in carcinoma of the stomach.

I would further emphasize one point in particular that was brought out by Dr. Pfahler, and to which Dr. Anders has alluded, and that is in regard to the radiographer being supplied with the essential clinical data in connection with the case to be examined. In perhaps half the instances in which cases are referred for chest and abdominal examinations the radiographer receives very little clinical data, or even none at all, to assist him in deciding upon the best way to go about examining the patient. For example, in a renal case he may be simply asked to look for a possible stone, or in another instance an examination of the stomach is requested, and little or no information is forthcoming as to any of the possible conditions whose presence is suspected. Anyone who has been present during Dr. Pfahler's demonstration can readily understand the extreme importance of the *x*-ray examiner being thoroughly familiar with the clinical aspects of such cases as have formed the topic of the paper just presented. Without such a foundation upon which to work, the examiner may easily overlook many things of importance, or at least much valuable time may be lost.

Dr. Charles Lester Leonard: Dr. Pfahler's demonstration has shown, I think, that it is possible to determine by the *x*-rays the encroachment of any growth upon the lumen either of the esophagus or that of the stomach; but, it is impossible for us to determine the etiological factor. There may be conditions which will give indentations in the shadow corresponding, and similar to those of other more malignant forms of disease, and yet we can only determine the fact that there is some foreign growth present, some abnormal condition which encroaches upon the lumen of the stomach. In a paper presented before the college some time since I showed that the form of the peristaltic wave in the stomach varies according to the condition at the pylorus, that where there is obstruction we have a wave of greater volume, and in a like manner any injury to the motility of the wall of the stomach can be shown. In this study of the motility of the stomach by the skiagraph the failure of motility at certain points will indicate the presence at those points of disease which has injured the musculature of the stomach, but I doubt if those early beginnings of malignant disease which encroach only upon the mucous surface of the stomach will be shown to any marked extent. The abnormal form of the wave will show us the commencement of obstruction at the pylorus and will lead to early diagnosis of malignant disease commencing at that point. I believe, as has been said by a number of speakers, that early examination of the stomach in these conditions will lead to an early recognition of disease at a time when operation is of value.

Dr. Pfahler, closing: We, of course, will not be able to diagnosticate all carcinomas of the stomach, but I do believe that we can show by a great deal of patience and in time the majority of carcinomas of the stomach before they are palpable, and that is a step in advance of any of our clinical methods today. There still will be a great many, as has been said, that you cannot even feel when you get your hands on them, and which we cannot show. I believe that the majority of carcinomas about the pylorus can be demonstrated before they are palpable. Those attacking the greater or lesser curvature will be more easily shown than any other. Those attacking the posterior or anterior wall are most difficult because you have a superimposed shadow. These can be demonstrated only at certain stages of the filling of the stomach. I spend hours on the examinations extending over a period of two or three days. With care and patience the majority will be shown before they can be demonstrated by clinical methods.

THE LAW OF DEGENERACY IN ITS RELATION TO MEDICINE.[1]

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Degeneracy or the degeneration of man has usually been considered conventionally; that is, as being equivalent to moral perversion; and its manifestations have been discussed more especially with reference to criminals and sexual perverts. It is at once evident that a degree of moral degeneracy less marked than that which leads to breaking the statute law or than which leads to sexual perversion is still degeneracy; it is a matter of degree and not of kind. Upon analysis it is found that moral degeneracy in its various degrees is merely a less or greater degree of selfishness.

As man has an intellectual and a physical as well as a moral nature, and if degeneracy is to be considered in a philosophical instead of in a conventional sense, it is apparent that intellectual and physical degeneracy must also be considered under the general term degeneracy or degeneration. The extreme type of intellectual degeneracy is the idiot, whether this be of hereditary or acquired origin. The lesser degrees are the persons with a small head and heavy body; in other words, of the microcephalic type; and in a still lesser degree it embraces persons with dull intelligence. The various types of insanity, and also mental instability, are different manifestations of intellectual degeneracy.

Physical degeneracy exists under many forms or manifestations. The dwarf, the feeble individual, the chronic so-called nervous

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invalid, the sufferer from so-called chronic malnutrition, are some of the types of the physically degenerate. In a philosophical or absolute sense, all men who are not vigorous, healthy, and physically normal are to a certain degree degenerate or defective; and physical degeneracy embraces every type from the man who is slightly atypical to the most extreme degree of degeneracy which is apparent to all.

The question naturally presents itself as to whether moral, intellectual, and physical degeneracy bear any relation the one to the other. As the brain is the organ of the mind and the seat of the intellect as well as of the moral nature, and as the brain is a part of the physical body, and as the activities of the brain in the intellectual and in the moral world depend upon the integrity of the brain itself and its various parts, one would infer upon *a priori* grounds that the different varieties of degeneracy are related the one to the other, and that intellectual and moral degeneracy have as their ultimate foundation aberration in the physical and vital state of the brain. It is the purpose of this paper to point out the evidence that this indication is true and to consider more especially the bearing which this fact has upon medicine.

It is accepted by scientists that the evidence in support of the theory of evolution is satisfactory, and that it is through evolution from the simple to the complex that nature as we now know it has developed into its present status. Among the laws of nature which have a profound influence upon living organisms, including man, is the law of natural selection, as it was named by Darwin, or the law of the survival of the fittest, as it was termed by Herbert Spencer. It is through the workings of this law upon living organisms that the fit or the strong survive, and that those organisms which are less strong or less fit are crowded out or cease to exist. It is by means of natural selection that the various genera and species (including man) not only maintain their existence, but also their characteristics; that is, they remain relatively stable from generation to generation in their form and function. So far as the human is concerned, this takes place through the action

of the laws of heredity and of environment, typically when the fit intermarry with their kind, and less typically when marriage takes place between opposites, the children of such marriages developing under relatively normal environment. The biological process whereby this comes about does not concern us in this connection.

We are more especially concerned with the question as to how the unfit or the weak have ceased to be the strong or the fit. This is most easily demonstrated in the vegetable world. Let us take the case of the annual plant or weed which develops in good soil under favorable conditions. It is well known that under such conditions a multitude of seed germinate and begin to develop; that is, to undergo evolution from the seed to the full-grown plant. Certain of these plants grow more rapidly than others, and soon receive as a consequence more sunlight and more air, and through the processes of plant life their development or evolution is favored at the expense of those plants which are relatively shaded and deprived of sunlight and air. In due time a certain number of the plants attain their full growth or evolution, whereas others, because of the lack of sunshine, air, and sufficient nutriment, are relatively stunted, do not reach full development, or it may be said they are instances of arrested evolution or imperfect development, or developmental hypoplasia, which is the term which we shall employ to designate this condition.

For the plants which we have been considering the environment has been good—that is, the condition of the soil, moisture, and sunshine. The question as to why certain of these plants grew more rapidly than others we shall not attempt to solve fully, but shall merely indicate that while this may have been due in part to environment, it may also have been due in part, at least, to a difference in the seed. Every agriculturist and every horticulturist knows that in a given soil the quality and the quantity of the crop depend upon the character of the seed, so that problems both of heredity and of environment enter into the situation which has been discussed.

The problem is simpler if we consider the annual plant or

weed which develops in poor soil with unfavorable conditions as to moisture and as to sunlight. The first year such a plant or weed grows up and is evidently not in a normal or healthy condition, it is yellow instead of green -that is, it is deficient in chlorophyl, which is the life-giving principle in the plant. The following year in the same place the plant is not only yellow (that is, deficient in chlorophyl) but also very spindling. The third year it is dwarfish and stunted in appearance as well as yellow; and the fourth year, if such a plant comes up at all, it is very dwarfish and yellow and fails to develop seed which can germinate; that is, the particular line of life disappears. The problem as studied in this connection is very simple; through heredity and environment in three or four generations the line of life has ceased. Chlorophyl represents the life principle or vital force or vitality of the plant, in which the plant of the first year considered was deficient. This state in the plant is the analogue of physical degeneration in animals and man. In each succeeding generation the seed of the degenerate plant contains less and less of the potential of life which is necessary to give rise to a normal plant. The process is hastened and largely influenced or controlled by environment. The plant which we have considered represents the unfit in the vegetable kingdom, and the biological process whereby from generation to generation through environment and heredity it became progressively less and less perfect or more and more degenerate until the power of germination became lost is that of degeneracy. In other words, the law of degeneracy is that which controls the biological processes, whereby the fit become the unfit, the strong become the weak, and in the course of three or four generations a particular line of life dies out.

Through the law of natural selection, a part of which is that there is a tendency for opposites instead of similars to intermarry, there comes, through the intermarriage of those of degenerate stock with those of better stock, an infusion of better blood; and when the offspring of such intermarriages are brought up under relatively normal environment, in the course of four generations,

more or less, the offspring of degenerate stock may be brought back to the normal or relatively to the normal. Thus, the status of the genus and of the species remains relatively stable, because through the law of natural selection the strain or line of life remains normal or is brought back to the normal when the fit intermarry with the unfit; or through the law of degeneracy when degenerates intermarry, the particular strain or line of life disappears in three or four generations, and thus fails to affect longer the general average of the genus or species.

The laws of nature are inevitable in their action. When an organism is subjected to unfavorable environment, involuntarily in the case of plants and domesticated animals, and more or less voluntarily in the case of man, degeneration results; and when the conditions persist from generation to generation without a change of environment and without an infusion of new and better blood, the line of life disappears through loss of procreative power—through the failure to form seed capable of germination in plants, through the loss of procreative power in animals, and in man also through moral perversion in deliberately providing against the propagation of the species.

Overcrowding, poor soil, unfavorable conditions as to moisture and sunlight, represent bad environment in the vegetable kingdom. Domestication and relative starvation represent bad environment in the animal kingdom. And civilization, more especially in its extremes of riches and poverty, represent bad environment for man. In the one (the rich) bad environment is voluntarily sought in the indulgence in luxury, idleness, the lusts of the flesh and the pleasures of the senses, and the failure to observe the law of development, which is that each member or organ can only develop through normal use, and that without it it remains undeveloped, or, when developed, it undergoes degeneracy. In the other (the poor) it is involuntary, and degeneracy is caused when through necessity inordinate labor is performed, or when sufficient or suitable nourishment is impossible of attainment.

It is of interest that the law of the beast or the law of the survival of the fittest is philosophically the law of selfishness. The beasts

have instinct, which guides their actions in their own interest. In man, selfishness is of two kinds—intelligent or reasonable selfishness, which is analogous in its action to that of instinct in beasts, and unreasonable selfishness, which leads to self-indulgence and to the oppression of others. In man, degeneracy is the outcome of unreasonable selfishness; in the rich through self-indulgence and in the poor through oppression and the denial by the employer to the employee of a sufficient remuneration to permit of normal living. Selfishness among the poor in its relation to degeneracy also takes the form of self-indulgence, more especially in alcoholic excesses. In man, the strong or the fit, relatively speaking, are the rich and the middle class, and the weak are the poor; but the unfit are found in all classes and are degenerates, whether this be moral, intellectual, or physical. And while selfishness is the philosophical principle which causes the fit to become the unfit, degeneration is the biological process whereby this is accomplished.

The natural man is the savage, to which the civilized man bears the same relation as does the domesticated animal to the wild or natural animal. It is a property of living beings in the course of generations to become more or less habituated to a relatively bad environment; that is, a species is evolved which is capable of living a normal life under conditions which were relatively unfavorable to the remote ancestors. In the evolution of this species, degeneration and pathogenic organisms cause in many individuals degeneracy, sickness, and death. This is the process which is going on with civilized man. The natural man lived in the open, and was obliged to take exercise in order that he might obtain the means of sustenance, which conditions are very different in modern civilization. Not only does man not live in the open at present, but instead, as a matter of fact, he lives more and more not only in houses, but also in urban communities. His habits of life are relatively less and less natural as civilization, or society, becomes more and more complex or artificial. Likewise, as a result of modern conditions, man is more and more subjected to strain and to irritation, no matter

which is the grade of society to which he may belong. Competition in labor, in business, and in the professions is more active than formerly. The railroad, the steamboat, the telegraph, the daily press, the telephone, and all of the various discoveries which are utilized in modern society tend to increase the burden which the nervous system has to bear in the modern man as compared with one who lived in a simpler state of society. These conditions lead to nerve strain, and this increases the resort to stimulants and narcotics; and overwork and overstimulation lead to degeneracy and to disease, the result being the special diseases or morbid states of civilized man which have come about through the law of degeneracy or degeneration.

It should be added that while the primitive natural man is the savage, in a certain sense, the civilized man is also the natural man — in other words, the civilized man is the developed or evolved savage. Much of the environment of the savage tended to the development of his physical well-being — his life in the open and the necessity for physical exercise. On the other hand, the lack of shelter, undue exposure to the elements, and the absence of proper nourishment at times were conditions adverse to normal physical life. In so far as civilization affords shelter under hygienic conditions, protection from the elements, and a normal food supply, it tends to the conservation of the physical well-being of man; but it acts in the reverse way in so far as it involves indoor life under unsanitary conditions and either luxury or undue poverty.

Conditions similar in their nature have brought about the diseases of the domesticated animals, because the domesticated animal likewise lives in an abnormal environment. It does not have to work for its sustenance in a natural way, and it is housed instead of living in the open; that is, it lives under relatively unsanitary conditions, with resulting degeneracy and loss of natural immunity.

Having seen that the diseases and morbid states of civilized man, speaking broadly, are due to degeneracy or to the fact that man has not been able to thrive under the particular environment to which he has been subjected, we will now consider what are

the special diseases of the civilized man as contrasted with those of the savage. The most prominent of these are: Tuberculosis; the surgical infections, including puerperal infection; the so-called functional neuroses, including trophic changes in the body; the so-called functional indigestions with their associated auto-intoxications; and degenerative changes in the bloodvessels, kidneys, and liver, which presumably bear the relation to the former of effect to cause; and cancer.

Man is evolved from the ovum. The ovum is potentially man, as by evolution the ovum becomes the adult man, the resultant man being the product of heredity and environment, development or growth taking place in accordance with biological laws. The impregnated ovum having a normal line of ancestry, and developing or evolving under normal environment, results in a normal adult man. As man has a physical, an intellectual, and a moral nature, and as the ovum is potentially the adult, it follows that the ovum represents potentially the three natures of the adult man.

We are taught that something does not come out of nothing, and also that we cannot give that which we do not possess. The bearing of this upon the impregnated ovum having a degenerate line of ancestry is apparent. The conditions are the same as when the poor seed of a plant falls upon poor ground under unfavorable environment, which results, as we have seen, in the plant which is deficient in chlorophyl, and which annual plant degenerates from year to year until it disappears in three or four generations, in accordance with the law of degeneration. Just as the plant was deficient in chlorophyl or the life-giving principle, so is the physically degenerated man and woman deficient in life force or the vital principle, or (as it is said) "they have a low vitality;" as they do not possess full life or normal vital force, they cannot transmit it to the next generation. The resultant impregnated ovum is potentially defective or degenerated, and the adult evolved from such an ovum is likewise defective or degenerated physically, intellectually and morally. The degree of the defect is dependent upon the vital force or principle or energy received into the ovum,

modified more or less by the character of the environment of the particular individual. The nature of the force or vital energy which causes the unicellular ovum to evolve into the normal human adult is not understood, as it is life itself, the essential nature of which is unknown; we only know so much of it as can be appreciated by our senses in its manifestations. It is evident, however, that the evolution or growth of the ovum to the adult takes place according to natural or biological laws, and that a relatively unfavorable environment interferes with this evolution or growth, and results in arrested evolution or imperfect development. This arrest may take place at any period, whether in the embryo, the fetus, the child, the adolescent, or the young adult, and the result is developmental hypoplasia.

It is not our desire in this connection to trace the relationship between degenerate ancestry and the morbid conditions and death of the embryo or fetus and the child.

Throughout both the evolution, or period of development, and the involution, or the old age of man, degeneracy can be acquired. In other words, degeneracy is both hereditary and acquired. In the period of evolution it results in developmental hypoplasia, which may be so extreme as to lead to death, and in the period of involution it hastens involution, which is another way of saying that it causes premature senility, and thus is a contributory cause to the death of the individual.

The subject is so large that it will be necessary to deal with it here merely in outline. If the defect in vital force or vitality of the ovum is extreme, the death of the ovum and abortion results. If less extreme there results monsters, spina bifida, cleft palate, harelip, deficient members, etc., or an imperfectly developed fetus; or the defect may be more manifest in a certain portion of the fetus, and result in congenital idiocy, imbecility, or dulness of intellect in the child, the microcephalic type of idiot, or person with dull intelligence. The relationship between developmental hypoplasia and the so-called nutritional diseases of infancy and childhood must be passed over for separate consideration. In this connection, reference will be made only to

the manifestations of degeneracy in the school child. One type is that of the various degrees of dulness of intellect; the opposite type is the unnaturally bright child with a relatively frail or feeble body — the so-called neurotic child — in which the defect has been most manifest in the muscular and circulatory and other general structures of the body, and less manifest in the nervous system. The so-called nervous children, that is, those having an unstable nervous system, form a group between the dull children with heavy bodies and the bright children with frail bodies.

Arrested evolution becomes more distinctly manifest at the period of puberty. This is more true of girls than of boys, as the evidences of puberty in girls are more apparent. The usual signs of puberty fail to appear; the body retains the form of the child, that is of the neuter; the frame does not broaden; the roundness of the body and its various members, due to the deposit of fat, which characterizes the maiden, fails to develop; the pubic hair does not grow; the breasts remain undeveloped, and menstruation fails to appear. In the more marked cases the arrest of development is universal; it affects all the tissues of the body and is not merely an arrest of development of the sexual organs. It is equally true of the bones, of the muscles, of the circulatory organs, of the nervous system, and of the glandular structures. In other words, there is a general developmental hypoplasia. Except in those of the idiot type, its more prominent manifestation is in relative debility, nerve instability and anemia, which under these conditions is called chlorosis. The least manifestation of it is nervous instability, a relatively slender figure, and the undeveloped cervix with a small os, the so-called "pin-hole" os of Marion Sims, with associated dysmenorrhea of the so-called nervous or ovarian type. This group of women is relatively sterile. When they marry and do not become pregnant, frequently they worry over this personally and also worry their husbands and the doctor, and develop nervous prostration as a consequence; or, if they become pregnant, all of the nervous symptoms of pregnancy are exaggerated, and in labor they suffer inordinately, and tend to become exhausted; hence in this group it is usually

necessary to resort to artificial delivery. Because of the imperfect development of the cervix and pelvic floor, lacerations are the rule, and in many of them puerperal infection results, which has been attributed in the past to exhaustion due to the serious labor. The forces of labor are imperfect because of the maldevelopment of the uterus, and of the nervous system, and the exhaustion has the same cause. Infection results because of relative loss of immunity with reference to the pathogenic pus-producing organisms. Usually these women are much prostrated and do not make good recoveries from labor, and many of them develop nervous prostration.

This same group, and this is equally true of the degenerate man, is much more apt to suffer from the surgical infections than are normal individuals, because of the loss of relative immunity. Notoriously it is the group which develops post-operative infection of the urinary organs.

Degenerates in whom the degree of arrested evolution is sufficient to prevent the development of the adult body form are those in whom tuberculosis is common. The neuter type of body is slender, the curves of the vertebral column are altered, the chest is flat, the abdomen protuberant, the muscles and ligaments atonic, presenting the appearance in motion as though the joints are "tied together with yarn strings." They develop tuberculosis for the same reason that they develop the surgical infections. It is due to relative loss of immunity.

The same group, that is, those having the neuter type of body with hypoplasia of all their tissues, develop the visceral ptoses—the so-called Glenard's disease—which includes ptosis of the stomach, intestines, liver, spleen, kidneys, and pelvic organs. These ptoses are due to one of two causes. The first is arrest of development in fetal or child life, which may prevent the various organs not only from reaching their full size, but also their normal position in the body; thus the kidney may be found in any position, from the pelvis to the lumbar region, never having ascended as it normally should; likewise the position of the colon and the stomach may never have altered from that which is normal in the fetus

to that which is normal in the adult. Such ptoses are more properly considered as embryonal types of position; they have not dropped from a normal position, but have never assumed in the development of the individual their normal adult position.

The second cause of the visceral ptoses is the lack of tone in the tissues of the body. Owing to the alteration in the configuration of the spinal column, and to the lack of tonicity in the abdominal muscles, we have an altered configuration of the abdominal cavity with loss of normal force or pressure exercised by the muscles of the abdominal and pelvic walls, which, together with respiration, affords, in the normal individual, a conservative influence in maintaining the position of the abdominal and pelvic organs. This force is altered and distorted and becomes more or less a destructive instead of a conservative force. The lack of tone of the tissues of the body due to hypoplasia prevents the normal supporting ligaments from giving adequate support to the various organs concerned. The resultant of these conditions is visceral ptoses.

The influence of degeneracy upon the nervous system, which includes the brain, the intellect, and the moral nature, is even more manifest than is true of the body in general.

The extreme type of inherited degeneracy of the intellect is the so-called congenital idiot, and its lesser degrees are the imbecile, the person of slight intelligence, and those of dull intellect of the idiot type. These have the microcephalic type of head, with the relatively heavy body of the idiot. Mental and nervous instability, when hereditary in origin, are merely lesser degrees of degeneracy. All of these forms of intellectual degeneracy are due to hypoplasia of the nervous system.

The so-called functional nervous diseases, insanity, epilepsy, catalepsy, hysteria, nervous instability, and nervous prostration, when due to degeneracy, are other manifestations of hypoplasia of the nervous system, and are due to varying degrees of hyperplasia or imperfect development of the protoplasm of the brain, spinal cord, and nerves.

The nature of cancer is a problem only second in importance

to that of tuberculosis. That cancer is due to degeneracy, or is a product of civilization, is indicated by its relative frequency in civilized man as compared with the savage, and by its increasing frequency. This induction is equally applicable, whether cancer is due to a parasite or is embryonal in origin. The full-blooded Guinea negress almost never has cancer of the womb, whereas it is common in the degenerate mulatto. The frequent relation between cancer and tuberculosis in the same family is equally suggestive. Much more study is requisite in order to demonstrate the hypothesis that cancer is a product of degeneracy.

Degeneracy may be acquired as well as inherited. A bad environment may arrest the development or evolution of the growing child of normal ancestry and result in developmental hypoplasia. The condition is similar, if not identical, to that when it is of hereditary origin. The acute infections, bad sanitary conditions, and malnutrition the result of improper food are among the chief causes of acquired degeneracy or arrested evolution. In the case of children and young adults this point is emphasized, in order that it shall not be inferred that developmental hypoplasia is always hereditary in origin. In the adult, the chief causes are overindulgence in food and drink, sexual excesses, and overwork, in addition to those causes operative in the young.

The essential nature of developmental hypoplasia and of involutional hypoplasia is a subject the discussion of which must be deferred, and in this connection it will merely be stated that the condition is evidently due to an alteration in the nature of the protoplasm of the tissues of the body.

Degeneracy which is acquired by one who has already become an adult (that is, who has fully evolved to the adult type), as is true of the individual in process of development, may affect the physical, intellectual, or moral nature. It is due even more to environment than is true when degeneracy occurs in the young, and is frequently due to the bad habits of the individual. The law of growth or of development is that the part or organ, or the organism as a whole, must be employed or must work upon normal lines, in order to develop or to maintain a degree of develop-

ment already acquired. The lack of use or overuse of a part or of the whole results in degeneracy; hence idleness, luxury, indulgence in the lusts of the flesh or the pleasures of the senses, on the one hand, or deprivation of the normal amount of nutriment or overwork, on the other hand, causes degeneracy either in the organism as a whole or in some of its parts. Arterial degeneration, heart disease, and degenerative changes in the liver and kidneys are some of the consequences of acquired degeneracy. Hypoplasia of a more general character is the result of chronic malnutrition.

It is evident that just as the effect of degeneracy upon the individual in the period of growth is to arrest the evolution or development of the individual, so in the individual who has passed early adult life it has the effect of hastening his involution; or, in other words, of bringing about premature senility, and thus is a contributory cause of death.

In order that the practical bearing of the relation of degeneration to medicine may be rendered more clear, a few illustrations will be given. It was the study of the fundamental nature of delayed puberty which led me to realize that the law of degeneracy is the controlling force at the base of many so-called diseases or morbid states, and also led me to use the term "hypoplasia" as an explanation of the status of the tissues of the degenerate. Let us take the malpositions of the uterus from the standpoint of diagnosis and prognosis, and more particularly retropositions. These are either developmental in their origin, or they are acquired, or they may be mixed. It is well known that a certain group of women having retropositions of the uterus have numerous symptoms which have been regarded as due either to neurasthenia or to hysteria; and also certain of them have local symptoms which are direct in their nature, and they also may have certain reflex symptoms in remote portions of the body. In the past, it has been said that the local and reflex symptoms are directly due to the malposition of the uterus, whereas the neurasthenic or the hysterical symptoms are due to these general so-called functional nervous diseases; and it has been held that to cure

the woman anatomically will cure the local symptoms, but will not cure the hysteria or the neurasthenia. The relative accuracy of diagnosis and prognosis has depended upon the ability of the physician to differentiate between hysteria, neurasthenia, direct symptoms, and reflex symptoms in the past. In the light of our knowledge of degeneracy such a case should be studied in order to determine whether the woman is a degenerate of hereditary or of acquired origin, or whether she is of normal ancestry and has had a normal development, but has acquired a local disease. The family history; the history of childhood and of puberty; the body form, whether that of the adult or of the neuter; the presence or absence of the so-called stigmata of degeneracy; these will determine whether or not she is a degenerate. If a degenerate, she has hypoplasia of the tissues of the body, and the malposition of the uterus is merely a complication of the general state; whereas, if she has been a normal woman, she merely has a local disease. In this case, to cure the displacement of the uterus will restore her to health; whereas, if she is a degenerate, the uterus may be restored to its anatomical position, but she is still a degenerate and will still suffer from its manifestations, more especially from debility, from lack of physical vigor, from a tendency to the neuroses, or from various neuroses which have developed; and in order to benefit her it will be necessary to treat her along nutritional lines, and thus to modify and improve the defective protoplasm in the cells of her body.

The same set of facts applies even more clearly to the other ptoses of the body and is the explanation of the great difference in reported results and in the expression of opinion concerning the value of the various operations for the visceral ptoses.

The length of this communication prevents a more detailed reference to the other morbid conditions, but a few words will be added as to the bearing of the theory upon the prevention of some of the evils of degeneracy. If the human family could be dealt with as is true of animals, degeneracy could be prevented by forbidding degenerates to propagate their kind. This was attempted in a modified way by the ancient Spartans. It is not

for me to say that it is practicable at this period. It is evident, however, that when degenerates intermarry, their offspring require the very best environment, in order that the inevitable consequences of such heredity may be minimized. They should grow up in the country and live as near to nature as is possible. Their education should be different, and they should be discouraged or prevented from taking up indoor occupations, and should be discouraged from attempting careers involving great and continuous expenditure of nerve force. They are the unfit, and are unable to withstand the vicissitudes which can be successfully withstood by the fit or the strong. They should expend no more energy than they produce, and therefore should lead the quiet life close to nature in order that the income and outgo of nerve force may be equalized, and that they may live, as it is called, healthful lives. The relation of these facts to public sanitation and State medicine and the duty of the family physician in controlling or advising the lives of the young needs only to be indicated in order that it shall appear how fruitful this field is for future development.

REPORT OF A CASE OF RESECTION OF FIVE FEET OF INTESTINE FOLLOWING THROMBOSIS OF THE MESENTERY, WITH REMARKS UPON THE DIAGNOSIS.[1]

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E. M., single, aged twenty-eight years. A tall, poorly nourished mulatto woman, admitted November 14, 1908, to the Presbyterian Hospital, with severe cramps in lower abdomen, both sides, accompanied by nausea and vomiting of greenish material, beginning suddenly twenty-four hours before. The temperature was a little below normal; the pulse 60 to 70 and of fair volume; the leukocyte count was 9200; there was no local muscular rigidity; the whole abdomen flat and rather tender. The bowels had moved within twenty-four hours.

There was a history of disease of both tibias at the age of twelve. There were present scars of old ulceration on both legs with anterior bowing, probably congenital syphilis. Seven years ago a suppurating ovarian cyst of the right side had been removed at another hospital and a sinus which remained had been closed by operation nine months later at the same institution. There was a history of occasional attacks for some years of pain with vomiting relieved after two or three days.

In spite of the severe pain and vomiting present on admission, the comparative absence of signs of severe trouble, especially the good pulse, made it seem advisable to await developments.

[1] Read February 3, 1909.

In the next forty-eight hours there was frequent vomiting of watery mucus, with occasionally a bile tinge, no blood, no fecal odor, very severe, general pain, at first intermittent, then constant. Absolutely no distention. General tenderness of abdomen most marked on the right made examination unsatisfactory, but no local swelling or enlargements and no relative muscular rigidity could be made out. Efforts to get a movement of flatus or feces through the bowels entirely failed. Temperature normal or below, respirations normal, but the pulse gradually lost volume and tension, became accentuated; the rate from 96 to 112. Slight distention now began, and under the diagnosis of intestinal obstruction of obscure type the abdomen was opened an inch to the right of the old scars forty-eight hours after admission.

November 16, 1908. Operation, assisted by Dr. Geo. M. Laws. Thin, dark, watery fluid in peritoneal cavity, a few ounces. No lymph. No general adhesions, but a few easily separated about broad ligaments, especially to right. Nothing in pelvis to account for symptoms. Many coils of ileum purplish black and distended somewhat. Peritoneal coat smooth, but lacking lustre and œdematous. On delivering these coils the mesentery was found thick, purple, swollen, and rather rigid, as though from blood stasis. On under surface at two points sensation as of hard thrombosed vessels. Two narrow adhesion bands were severed, which seemed to partially obstruct bowel. Well-organized adhesion of bowel, size of pencil, to upper part of old scar. No sharp line of demarcation of the dark color, which involved the upper portion of the mesentery and about five feet of upper ileum and jejunum. Clamps were placed on healthy bowel above and below and the intestine rapidly trimmed off the mesentery near its border, except at one point, where a portion about two inches from edge, which was more firmly infiltrated with blood, was cut away. From the cut edges much venous black blood drained, a few oozing points were controlled by catgut stitches, put in with round needle. The ends of the bowel were united by two rows of Pagenstecher thread after the manner of Moynihan. The redundant mesenteric folds had now drained largely of blood, were much smaller,

and were folded over upon themselves after Kocher's method. A cigarette drain; wound in abdomen nearly closed. Fowler position. Murphy salt solution by rectum.

There was much adynamia, but no peritoneal infection. The low vitality of the patient caused an absence of attempt at union of the parietal incision, the lips of a dark gray color falling apart down to the peritoneum when stitches were removed. Intestinal wall floored this depression. There was no leakage at the site of anastomosis, but a small fistula formed in the exposed intestinal wall about the seventh day. This was apparently caused by sloughing out of a small infarct. After operation there was little fever and no vomiting at all. Flatus passed in twenty-four hours. Bowels moved freely and naturally by anus after fourth day, with tendency to diarrhœa. Nutritive enemata were at first used instead of food by the mouth. Great improvement in strength followed use of iodide of mercury, after convalescence was established.

[Addendum: Six months later the bowel fistula was closed successfully by resection of its site and end-to-end anastomosis. The patient remains well.]

The above is a typical picture of the conditions described as thrombosis of the mesentery. The purplish-black color was different in shade from the black of strangulation and the peritoneum looked more edematous or sodden. There was no sharp line of constriction at the site of the bands, but the discoloration continued beyond them and shaded to the normal. The bands probably did not completely occlude the bowel, but as in the attacks in previous years, only as the bowel distended did they interfere. The primary condition was thrombosis. The distention was very late and secondary.

Strangulated portions of omentum may show large sac-like accumulations of bloody fluid. Moynihan mentions a case of volvulus associated with a distinct tumor which was removed with the bowel and afterward proved to be blood alone, but there is nothing except occlusion of mesenteric vessels which is capable of giving such extensive hemorrhagic infarcts with diffuse swelling in the non-strangulated mesentery.

Not many cases show the slow development of distention and pulse change which my patient showed, but if they do in the presence of severe pain and vomiting, a diagnosis of thrombosis is more likely than one of acute strangulation. In many cases of thrombosis, however, the development of distention and secondary peritonitis following the attack by organisms upon the engorged tissues is so rapid that it is not possible to separate the primary disease from mechanical ileus or from the so-called dynamic ileus.

The condition must be separated, says Eisendrath, from acute peritonitis associated with cholecystitis or appendicitis and from intestinal obstruction, from torsion, bands, intussusception, hernia, etc. From acute pancreatitis, lead or renal colic, and torsion of tumors. Referred pain from pneumonia or pleurisy, especially diaphragmatic pleurisy, must be considered. Each of these conditions has symptoms of its own and can usually be differentiated. Thrombosis or embolism of the mesentery may, however, appear secondarily to any inflammation along the portal or mesenteric vascular systems, so that appendicitis, for example, may be thus complicated.

The various causes of embolism elsewhere apply here. They include disease of the heart valves or of the bloodvessels, syphilis, arteriosclerosis, or vascular traumatism.

The outcome is usually fatal, though collateral circulation has in a few rare instances been reëstablished; 94 per cent. are said to die. The only hope is in resection of the intestine, but operations are said to be very discouraging and few recover. Of 47 operation cases quoted by Jackson only 4 recovered. Even very small emboli in terminal branches may cause small perforations of the intestine when all else is well.

As to the method of operation, Moynihan considers that all cases should have the diseased part rapidly cut away and an artificial anus established without an attempt at anastomosis, owing to the difficulty in telling how far the gangrene will ultimately extend. In the case reported the anastomosis was success-

fully completed, though a small fistula arising at another point remained until closed by later operation.

The evidence of thrombosis before operation was not clear, nor does an after study of the symptoms do more than show that they were consistent with such a condition, while not excluding slowly progressive ileus from chronic causes such as bands.

The diagnosis of thrombosis is always uncertain and usually impossible. It is likely to remain so because types of cases vary greatly. In one type there are copious bloody stools with diarrhea, and if the higher branches of the superior mesenteric vessels are involved, there may be bloody vomiting. On the other hand, many cases, such as this one, show absolute impermeability of the bowels, and no blood is seen. The sudden agonizing and continuing pain is a marked feature, and is never absent, but pain is common to nearly all acute abdominal conditions and is not diagnostic. Hemorrhage when it occurs is very suggestive, but it is hidden when the bowels do not move. Only in the rare, slowly progressive forms can more common causes of ileus be probably excluded. There is no symptom group which really serves to make the diagnosis, but fortunately operation is indicated in practically all of the conditions for which it might be mistaken, and operation is the only hope.

There is little help to be obtained from locality of symptoms, as these vary so greatly according to the extent of the infarct and to the branches of the superior or inferior mesenteric vessels primarily or secondarily involved. The amount of bowel imperilled varies from a narrow ring-like band produced by the occlusion of a terminal branch to a large part of the small intestine with portions of the large. The area is extended if the portal system is invaded.

AN ACCOUNT OF THE SUBCUTANEOUS INJECTION OF SEA WATER AND RESULTS OBTAINED.[1]

By THEODORE Le BOUTILLIER, M.D.

The benefit derived from the use of sea water and sea air has been known and utilized for generations. These, in recent years, have been made use of in the treatment of tuberculous disease, notably that of the bones and joints. The many hospitals and sanitaria situated on the sea coast prove conclusively the benefit which is to be derived from their use.

The internal use of sea water by subcutaneous injection has been studied for upward of ten years on the continent, particularly in France.

Quinton discovered that by diluting sea water a solution could be obtained that was isotonic with blood plasma, and in which, when kept at blood temperature, the leukocytes continued their ameboid movements for several hours. In experimenting with artificially made solutions the results obtained were not so perfect.

This work was suggested by the now universally accepted theory of the marine origin of life. In each series of life, from the lowest organisms to the highest, he observed a close correspondence of the chemical composition of the plasma with that of sea water. To quote what Quinton calls "Loi de constance marine originelle," or the law of the constance of marine origin, which reads, "Animal life which appeared as a cell in the sea has always tended to maintain for its high cellular function, throughout the zoölogical series, cells composing each organism in a marine medium." In other words, life having first appeared as a cell

[1] Read March 3, 1909.

in the sea, the cellular life of each organism in consequence reaches its best development in a marine medium. According to his experiments, which were careful and conclusive, nature has supplied this marine medium with great chemical exactness in the blood plasma.

In experimenting along the line of this theory, Quinton injected into a dog an amount of isotonic sea water equal to twice the weight of the dog. This caused no perceptible discomfort, with the exception that the kidneys were remarkably active, and by the end of the second day the dog was in a much better condition than previous to the injection. Secondly, he bled a dog until it reached the state of lividity, when warm isotonic sea water was intravenously injected, the quantity being equal to the amount of blood withdrawn. In a few moments the heart began to beat and the dog to breathe, while in a few days the dog developed a superabundance of life, with a most marked increase of hemoglobin above that which it had at the time of injection.

Chemical analysis of sea water and blood plasma proves that they contain the same minerals in almost identical proportion, the same being true of the various salts. For this reason one can readily comprehend that the injection of a solution containing elements in almost exact proportion to those of the organic fluids will have a very beneficial action upon the human organism, especially in certain diseases. In other words, body cells that are not obtaining sufficient mineral nourishment will have this supplied to them by the sea water, the action being distinctly tonic and assisting in the upbuilding of the cell itself. This marine serum ("isotonic sea water," or sea water solution) does not have any bactericidal action, but increases the cellular resistance to infection.

Experiments by Carrion and Hallion, in France, have proved that isotonic sea water has an entirely different action from that of physiological salt solution, that edema is never produced, and there is not the retention of chlorides, which has occasionally been found to be the case in the injection of physiological salt solution.

Robert-Simon notes in a paper[1] that various investigators have proved that isotonic sea water solution is superior physiologically and therapeutically to physiological salt solution, while Hallion, Quinton, and Julia,[2] and Quinton,[3] show that the kidneys eliminate twice as much in volume when sea water solution is used as with the use of physiological salt solution.

Moreover, Quinton kept alive the leukocytes of fish, reptiles, birds, dogs, rabbits, and man in sea water solution, which he could not do in any other artificial serum.

Overton (1904), experimenting with solutions of chloride of potassium, chloride of calcium, and isotonic sea water, found that the last is best suited to maintain the vitality and maximum force of muscular and nervous tissue.

Pouchet and Schabry, experimented with artificially prepared sea water, while Lyon evaporated sea water to dryness, redissolving it in pure water, but found the action was not at all the same. Tixir,[4] experimenting upon children with acute gastro-enteritis, using physiological salt solution in one series and isotonic sea water in another, found, at autopsy, in the bone marrow, a marked proliferation of cellular elements (myelocytes and eosinophiles). Further, that the reaction produced by these solutions is of the same nature, but that of the sea water is of more marked intensity. Mace and Quinton[5] further proved that the gain in weight in the debilitated newly born was almost twice as great per day with the use of sea water solution as with the artificial serum. They found that in cases where the artificial serum was without effect marked gain resulted from the use of sea water. Potocki and Quinton[6] give the same results.

Through the kindness of Captain Thatcher, of the "Indian," a boat making trips to Boston, I have been supplied weekly with sea water collected from the Atlantic Ocean, at a point about

[1] Bulletin Général de Thérapeutique, 1906, p. 288.
[2] Société de Biologie, 1897, pp. 1042 to 1063.
[3] L'éau de Mer, milieu organique, pp. 175 to 207.
[4] Bulletin, Société de pédiatric de Paris, 1908, p. 104.
[5] L'obstétrique, September, 1905
[6] Gazette des Hôpitaux, November 30, 1905.

forty miles from land and midway between the capes of the Delaware and Sandy Hook. It is collected from a depth of from thirty to forty feet, in sterile gallon bottles. The bottles are fastened in a heavily weighted rope basket and lowered rapidly so that very little of the surface water can enter. The water is best obtained in the locality of a sandy bottom, such as we have off the New Jersey Coast, and at the depth of thirty to forty feet, in order to obtain it as free as possible from the surface bacteria. The sea water is mixed in the proportion of eighty-three parts of sea water to one hundred and ninety parts of pure water, or about the proportion of two to three. This is filtered through a germ-proof Berkefeld filter and is put up in sterile bottles.

To quote from Robert-Simon:[1] One thus obtains an aseptic isotonic liquid, that is to say, of a molecular concentration equal to that of blood serum, of which the cryoscopic point or of coagulation is of 0.56. This is of much importance, since, because of this quality of perfect isotonicity of the sea water so diluted, we have a liquid which can be injected without pain, the only such one of a number of serums injected beneath the skin. The solution should be used within three weeks of the time of collection of the sea water, as it seems to be not so effective when kept longer.

Quinton[2] states that sea water sterilized in an autoclave at 120° C. loses its vital principle. The ameboid movements of the leukocytes cease. Injected into patients, it produces pathogenic effects, and in a dose of 700 grams injected into a dog caused death.

This solution, then, is put in a sterile glass flask, graduated in ounces, having a neck-like inlet at the top and a small side outlet at the bottom. A perforated rubber stopper, in which is fitted a sterile glass tube, is placed in the top opening, and when ready for use a bulb is attached to the glass tube. To the outlet of the bottle containing sea water for injection there is attached a sterile rubber tube some five feet long, on the end of which is

[1] Applications Thérapeutique de l'Eau de Mer.
[2] Bulletin Général de Thérapeutique, p. 379.

placed either a steel or platinum iridium-tipped needle (the latter being preferable). The needle used is about a No. 20 or 21; in other words, rather larger than a hypodermic needle, but smaller than an antitoxin needle. The site of the injection is either under the angle of the scapula or in the gluteal region. The needle is passed upward through the skin and superficial fascia, just above the sheath of the muscle. In the gluteal region it may be injected into the superficial fascia or fat. The choice of site of the injection is one mainly of convenience: In infants and young children the subscapular site is, I think, the best, while in adults the gluteal region is at times more convenient. The site of the injection should be washed with alcohol, the needle being sterilized by alcohol or flaming.

The amount injected varies with the age of the patient and the condition for which treatment is given: In infants and young children the initial dose is usually 15 c.c. ($\frac{1}{2}$ ounce), while it is rare to give over 50 c.c. In older children the initial dose may be from 15 to 25 c.c., going up to 60 c.c. (2 ounces). In adults the first injection should be 50 c.c., increasing in subsequent injections up to 100 c.c., at times giving as much as 150 c.c. (5 ounces). In acute cases, or serious ones, injection may be given once a day for five or six days, but, as a rule, an injection given regularly three times a week will be all that is necessary. The injection should be repeated in the same region, owing to the fact that the tissues have been relaxed and the solution enters more readily and without causing pain. Because the solution is isotonic, it is rapidly absorbed and very little pain or discomfort is experienced, with the exception of the first injection, when there may be some discomfort and tenderness due to the distention of the tissue. My first opinion was that there was very little difference in the action of the solution made in the proportion of two to three and that of equal parts. The former has specific gravity 1008, while the latter that of 1012. Upon more extended use however, a more painful reaction resulted in certain cases where the stronger solution was used.

The only reactions I found have been (1) a slight elevation in

temperature during the first six to twelve hours, followed by a rapid return to the normal, the fever, as a rule, occurring only with the first or second injection, with the exception of tubercular cases; (2) slight restlessness and more or less severe pain or brusing at the site of the injection. If the injections are too large in amount there may ensue headache, with a feeling of malaise, nausea, and, rarely, vomiting.

Some of the effects produced by injections of isotonic sea water are: Increase in appetite; improvement in cases of constipation; marked improvement in cases of diarrhea; increase in the quantity of urine eliminated; improvement in insomnia, and relief of functional dysmenorrhea. In cases of malnutrition, and in some cases of tuberculosis, the gain in weight has been marked. In cases of pulmonary tuberculosis, with cough and expectoration, it has been found that the expectoration ceased and within a few weeks the cough subsided.

REPORT OF CASES.

CASE I.—P. B., aged twenty-four years. Incipient tuberculosis. Had been treated for some months previously for a chronic cough, poor appetite, with marked constipation and insomnia. On December 10, 1908, sea water solution injections were commenced in doses ranging from 50 c.c. to 120 c.c. The first injection was followed by considerable pain and soreness at the seat of the injection, with slight rise of temperature. Following the third injection there was a decided improvement in the appetite and the constipation was less marked. Following the fifth injection much less cough and sleeping better. With the eighth injection the cough had entirely disappeared, she was sleeping well, and the bowels were moving normally without medicine. With each menstrual period there had been marked pain with scanty flow, and she was obliged to stop work for forty-eight hours. The period commenced on December 26, or sixteen days after the first treatment, and was without any pain or discomfort, she being able to work as usual. This has continued to be the case with each succeeding menstrual period. Treatment was continued three times weekly until January 11, since which time it has been given twice weekly. At present, although there has been no increase in weight, the patient is much improved in every way. She has no cough, has had no attacks of bronchitis or other illness, which is very unusual for her during the winter months, is very much stronger, and eats and sleeps well, while the bowels act normally.

Case II.—N. F., aged nineteen years. Incipient tuberculosis, accompanied by loss of strength, loss of appetite, insomnia, nervousness, hacking cough without expectoration, and acne vulgaris. This patient had been under treatment for over a year for the above. Isotonic sea water was first injected subcutaneously on December 7, the dose being from 50 c.c. to 120 c.c. Treatment was continued three times weekly. Previous to the first injection the temperature had been running a little over 99° in the evening, but since the fifth injection it has been normal. Following the first few injections there was a quite marked improvement in the acne, which, however, did not continue, it having returned to about the same condition as before treatment. The cough improved markedly and by the fourth treatment had entirely disappeared, the appetite and sleep were much better, and the nervous symptoms very much less. These conditions have gone on steadily until the present time. The gain in weight in this case has been three pounds, her gain in strength is very marked, and her general condition is much improved. When she was receiving from 100 to 120 c.c. we found that the insomnia returned, owing to overstimulation; this improved as soon as the dose was lowered. The variation in weight in this case was rather pronounced, some days showing a marked decrease, while at other times there was just as marked an increase.

Case III.—S. F., aged nine years. Pulmonary tuberculosis with hypertrophied tonsils and adenoids. Child first seen November 7, 1908. The mother has tuberculosis of the lungs, one infant has marasmus, three other apparently healthy children. The patient is said to have been always weak and sickly; she has had measles and pertussis. She gives a history of night sweats, is weak, and has a poor appetite; some cough with impaired resonance at right apex anteriorly and left base posteriorly; increased tactile fremitus and vocal resonance, and a few moist rales with prolonged harsh expiration. Skin dry and harsh. On December 12 her hemoglobin was 65 per cent., white blood corpuscles, 16,000. The first sea water treatment was given on December 15; on the 19th her weight was forty-five pounds, her appetite was better and cough less. On the 24th her weight had increased to forty-six pounds and on January 14 to forty-seven pounds, the cough having entirely disappeared at this time. She had an acute attack of tonsillitis, during which she was constantly under treatment, and on February 4 her weight had increased to forty-eight pounds. The Moro tuberculin test was positive. On February 8 her tonsils and adenoids were removed, and on the 11th examination showed normal resonance over the right apex and left base. The tactile fremitus and vocal resonance still slightly increased. Expiration very slightly prolonged. No rales on either quiet or forced respiration. The skin is soft and in good condition. There are no night sweats. The appetite is good and sleep normal. Her weight now being forty-nine pounds three

ounces. Blood examination, February 24, hemoglobin, 60 per cent.; white blood corpuscles, 15,600; red blood corpuscles, 3,720,000.

Case IV. F. F., aged thirty-five years. Pulmonary tuberculosis. Seen first, December 15, 1908, at which time marked lesions at the right and left apices anteriorly and posteriorly were demonstrable, impaired resonance, increased fremitus, many rales. There had been steady loss of weight and strength, with cough, expectoration, and pain in shoulders and chest until that time. She was given injections of sea water solution, starting with 50 c.c., which were increased to 120 c.c. These were given three times a week regularly. The only other treatment given was forced feeding, with milk, four quarts daily. The first improvement noticed was increase in appetite, followed by decrease in the cough and stoppage of the expectoration, marked improvement in sleeping and nervousness. At the present time there is no expectoration, the cough has entirely stopped, and her general health has almost reached the normal. Since December 1 she has gained eighteen pounds in weight, ten pounds being gained in the first six weeks. The apices of the lungs are normal, there being no rales, no impaired resonance or increase in fremitus, and expiration is not prolonged.

Case V.—E. M. E., aged three years. Pulmonary tuberculosis. First seen in August, at which time she showed marked evidence of tuberculous infection and malnutrition. There was practically no improvement in her condition, and on November 30 sea water treatment was started. During the four treatments between that time and December 7, she gained one-half pound in weight, her appetite had improved, she was much brighter, and her color was better. There was some slight malaise and fever following the first injection. On the 8th pneumonia developed in the right chest, and she died on the 13th, injections being given on the 9th and 12th.

Case VI.—J. Z., aged eleven years. Tuberculous periostitis. Family history negative. Patient healthy up to eight years of age, when she had tuberculous swelling of the arm and leg. Four weeks before first treatment the abscess was opened in the left thigh anteriorly, which communicated with the periosteum. The sinus was not healing, and it was thought the curetting of the bone would be necessary. She was referred from the surgical clinic for treatment on November 25. Examination showed a poorly nourished girl, with some impairment of resonance in the left supraclavicular fossa, no rales, no tubular breathing. On December 3 her weight was fifty-five pounds, at which time the first injection of 30 c.c. of sea water was given. Hemoglobin, 70 per cent.; white blood corpuscles, 10,800; red blood corpuscles, 6,120,000. On December 7 it was noted that the sinus was healing more rapidly than at any time previously, and that her general condition was better. On December 11, or eight days after the first injection, the sinus was completely healed, she had gained one pound in weight, it was noticed that her

color was much improved, she had a very good appetite, her bowels were normal, and she was sleeping well. On December 18, hemoglobin, 85 per cent.; white blood corpuscles, 11,200; red blood corpuscles, 6,250,000. She was discharged on December 23, after eight injections, with marked improvement in all conditions.

Case VII. B. C., aged ten days. Inanition and bronchitis. First treated on December 15 with 15 c.c., which was repeated on the 17th and increased to 20 c.c. on the 18th. It was noticed that following the first injection the infant took and retained the breast feeding much better and the bronchitis cleared up rapidly.

Case VIII. A. B., aged twelve days. Inanition and bronchitis. This infant received six treatments in ten days, from 15 to 30 c.c. being given at a dose, and here the bronchitis cleared up rapidly, while the feedings were much better taken and retained.

Case IX. B. W., aged five days. Inanition and hereditary syphilis. First seen December 16. Received seven treatments between the 16th and 26th of December, varying from 15 to 30 c.c. The appetite improved wonderfully, the stools were fairly digested, and there was marked improvement in the general condition.

Case X. B. B., aged five days. Inanition and hereditary syphilis. First seen December 16, receiving in all eight treatments between that date and the 28th, varying in amount from 15 to 50 c.c. sea water solution. When first seen the skin of the entire body was dry and fissured and had a parchment like feel. It was very thin, not feeding well. The appetite improved greatly and the change in the skin was remarkable, it returning to a perfectly normal healthy condition.

These four cases all increased rapidly in weight following treatment, but by an accident the charts were destroyed before they were copied.

Case XI. –C. C., aged eleven months. Malnutrition. First seen when seven months old during an attack of enterocolitis, at which time her nourishment was fair. There were slight rachitic signs. Weight, twelve pounds. When eleven months of age she had only gained one pound, and her muscular development was poor. When seen on November 30 she had marked signs of malnutrition, with fretfulness, enlarged abdomen, liver much enlarged, and marked separation of the recti. Her hemoglobin was 75 per cent., with red blood corpuscles, 4,570,000. She increased rapidly in weight, gaining one pound in the first eight days and another pound in the succeeding eleven days, or a total gain of two pounds in nineteen days. Her appetite improved,

the stools became normal, and her sleep was good. Since the last injection her improvement and gain has been constant.

Case XII.—A. S., aged eight years. Malnutrition. First seen January 13, 1909. She was brought for abdominal pain, constipation, and loss of appetite following measles two months previous. She showed quite marked emaciation, flabby muscles, skin harsh and dry, cervical, axillary, and inguinal glands all enlarged, rapid irregular heart action, marked pallor of lips and sclera. Blood examination showed hemoglobin, 85 per cent.; red blood corpuscles, 5,335,000. Weight fifty-two pounds. On the 16th she was given a subcutaneous injection of 30 c.c. of sea water solution, which was continued three times weekly until the present time, increasing the quantity to 60 c.c. Between the 16th and the 29th, or seven treatments, she gained four pounds in weight, and in the fifteen days succeeding has increased one pound. There is marked improvement in her appetite, the bowels are moving normally, her color is very much better, her skin has become soft and normal to the touch, and her blood shows very marked improvement. Blood examination: Hemoglobin, 90 per cent.; white blood corpuscles, 6600; red blood corpuscles, 6,248,000.

Case XIII.—H. D., aged eight years. Malnutrition. Brought for supposed tuberculous spinal disease. First seen October 5, 1908. Family history good, backward in speech, dull, apathetic, does not care to run and play with the other children, very nervous and easily frightened, skin dry and harsh. The Moro test, applied three times, gave no reaction. Tonsils and adenoids were removed on November 12. His general condition improved slightly up to December 3, at which time his weight was forty-two pounds, and the first subcutaneous injection of sea water was given. Hemoglobin, 75 per cent.; white blood corpuscles, 5200; red blood corpuscles, 5,130,000. Between the 3d and 19th, or during the first seven injections, the improvement was marked. The first sign noticed was a better appetite in the mornings, less nervous, and brighter; this was followed by more desire to play with other children and a quite marked improvement in his color. Blood examination on the 19th: Hemoglobin, 85 per cent.; white blood corpuscles, 14,240; increase of a pound and a half in weight. The next seven injections, or covering a period from December 19 to January 5, shows still more improvement in his general health, also a brighter mental attitude. During this time there was no increase in weight, the change in the skin condition was very marked, it entirely lost the harsh, dry feel, becoming soft and of normal moisture. Blood examination, February 20: Hemoglobin, 85 per cent.; white blood corpuscles, 12,000; red blood corpuscles, 4,128,000.

Case XIV.—H. L. T., aged seven years. Spasmodic cough for six months, which was unimproved by removal of adenoids and tonsils. Weight has been almost stationary for four months, there being also slight evidences of malnutrition. No signs of tuberculosis. Temperature normal, pulse

strong. The first injection given December 14, of 20 c.c., increasing to 50 c.c., in all eleven treatments, covering a period of twenty-five days. There was an increase of one pound and five ounces in weight, with better appetite and a brighter and happier disposition. Unfortunately the blood examination was not made until after the third treatment. Hemoglobin, 95 per cent.; white blood corpuscles, 9280; red blood corpuscles, 5,130,000. At the end of the treatment the hemoglobin remained the same; white blood corpuscles, 10,320; red blood corpuscles, 5,190,000. For a month following the last treatment he was in the country and in the open air continually, at which time the gain in weight was one pound and thirteen ounces.

Case XV.—M. K., aged fourteen years. Malnutrition. Complained of poor appetite, chronic constipation and marked weakness. Injections commenced February 10, of 30 c.c. increasing to 60 c.c. Very marked improvement after the third injection, appetite good, color much better, bowels moving regularly, feeling stronger. In fourteen days she received seven treatments and gained one pound and a half in weight. The condition of the skin, which was dry and harsh, has greatly improved. Hemoglobin increased from 75 per cent. to 85 per cent. in ten days.

Case XVI.—K. W., aged fifteen months. Marasmus. First seen December 2, 1908. Family history negative. In October, 1908, she was in the Municipal Hospital for two weeks with diphtheria, since then has had marked marasmus. She had a cough, with some difficulty in swallowing. General weakness and marked loss in weight, thirteen pounds and nine ounces. Emaciation, with dry, harsh skin, which hangs in folds on the arms and legs; so weak that she was unable to sit up, and only moved extremities slightly. Cry was one of weakness. Hemoglobin, 80 per cent.; red blood corpuscles, 4,410,000. Her weight varies between thirteen pounds fifteen ounces and thirteen pounds three and one-half ounces on December 26, since which time the increase has been continuous, until her weight is now sixteen pounds six ounces. She has had in all twenty-six treatments, varying from 15 to 60 c.c. in amount. As it had been impossible to get any food that would agree, she was sent into the hospital on January 7, where the treatments were continued until the 18th. The improvement in the digestion was slight, but the appetite was better and the stools contained less undigested particles. She had been kept in the fresh air constantly, and now her bowel movements are thoroughly digested. She is taking not only milk, but some solid food. The skin is soft and of normal consistence. She is bright and happy, not only sitting alone, but standing holding on to the crib, and can now even take a few steps alone. Although the gain in weight has been only about three pounds, the gain in muscular tissue and strength has been remarkable. Her cough has entirely disappeared and the chest is in a normal condition.

Case XVII.—D. F., aged five weeks. Marasmus. The infant of a tuberculous mother and with a sister who gives a tuberculous reaction, both of whom

are under treatment. He was brought on October 24 for an abscess on the right thigh, just above the knee, and a slight dermatitis. Weight, seven pounds. He was under treatment until November 25, at which time he weighed seven pounds four and one-half ounces, was still having frequent bowel movements, somewhat undigested and malodorous. Various kinds of food had been tried without success. He was sent into the hospital, receiving his first treatment on November 30 of 10 c.c.; this was given three times weekly until January 18, when he received his twenty-fifth injection of 60 c.c., his weight at this time being eight pounds and nine ounces, or a gain of one pound and five ounces. His ability to digest and assimilate food has increased. His strength has increased very much, while, instead of being fretful and peevish, he is happy and sleeps well. He also has been kept constantly in the fresh air. No injections were given from January 18 until February 8, when they were recommenced, since which time they have been given regularly three times a week. While there has been no gain in weight, his digestion is good and his general condition is improving.

Case XVIII.—M. P., aged eighteen months. Acute eczema of the scalp for one week. First seen December 8, when he was given 30 c.c. sea water solution. He returned on the 10th for his second injection, and on the 12th it was seen that there was very marked improvement in the eczema. It was almost entirely dry and the scales were coming off. Between the 12th and the 19th he received three more treatments, and on the 21st received his seventh and last, being entirely cured.

Case XIX.—J. A., aged eleven years. Eczema of the scalp and chronic indigestion. Injections ranging from 30 to 60 c.c. Following the second injection there was marked improvement in the condition of the scalp, the crusts had been removed, and the underlying surfaces showed much improvement. Practically cured after the fourth injection.

Case XX.—A. K., aged one year. Eczema of the scalp and furunculosis following pneumonia with malnutrition. The furunculosis has almost disappeared; the eczema has entirely healed. Six treatments were given, ranging from 15 to 30 c.c.

Case XXI.—S. G., aged nine months. Eczema of the scalp. Following the second treatment the scalp had cleared up and no new outbreak occurred; at the fourth treatment the head was normal.

Case XXII.—B. F. B., aged nineteen years. Acne vulgaris. First seen December 15; has been under constant treatment since that time; three treatments weekly, dosage ranging from 50 to 150 c.c. At times there has been marked improvement in the acne, no local treatment being given. These have been followed by lapses, but on the whole the condition of the skin is somewhat better; it, however, appears to me that it is of doubtful benefit in long-standing cases. The one point to bring out in this case is that this

young man has been subject to attacks of coryza or bronchitis almost every month during the winter; this year, however, he escaped all attacks and has been in better health than for many years, telling me that he feels more like work and study than ever before.

Case XXIII.—G. S., aged seven years. Chorea. First seen on December 28, 1908, at which time he had had choreic movements for two weeks, particularly on the right side; he was unable to feed himself, owing to the severe type of movement. Following the first treatment of 30 c.c. there was quite marked improvement; the movements were less, so much so that he could feed himself. By January 6, or following the fourth injection, we found that the movements had ceased. He received in all ten treatments, covering a period of thirty-one days; increased one-half pound in weight, and has had no return of the chorea.

Case XXIV. M. McG., aged thirty-five years. Leg ulcer, surrounded by atrophic area, due to an injury of one year's standing. Had been treated for two months previous to January 5, 1909, without improvement. Injections of 50 to 80 c.c. of sea water solution were given three times a week, until February 2, at which time the ulcer was not only healed but the atrophic area had practically regained its normal size and color. Local applications of sea water solution were used as well as the injections.

Case XXV. W. S. B., aged twenty-six years. Diabetes. An exceedingly bad family history, the grandmother on the maternal side, the mother, and a brother having died of this disease. The sugar had been varying between 4.4 per cent. and 5.5 per cent. He had frequent attacks of depression, but otherwise few symptoms. The quantity of urine voided varied from five to seven pints in twenty-four hours (80 to 112 ounces). Following injections of from 50 to 80 c.c., the urine first increased to eight pints (128 ounces) but gradually decreased to seven pints (112 ounces). The sugar showed a rather rapid increase, going from 4.35 per cent. to 5.06 per cent. and 5.88 per cent., which, however, decreased to 5.64 per cent. and 5.1 per cent. There has been a trace of albumin and a few hyaline casts. His general condition has been decidedly better, as during the month of treatment there has not been a single attack of depression and he has felt stronger and better in every way. No other treatment has been given with the exception that the carbohydrates have been cut down as much as possible.

Case XXVI.—K. L., aged three years. Typhoid fever. In the third week of the disease the temperature reached normal in the morning; pulse, weak and thready. Sea water solution of 15 c.c. injected February 17, followed by marked improvement in the pulse and general condition. Injections were given also on the 19th and 24th.

A few notes to summarize:

In the tubercular cases there has been a notable improvement in the general nutrition, evinced by increased appetite, regulation of the bowels, relief of insomnia, gain in weight, where there has been loss preceding, increase in strength, stoppage of cough and expectoration, and marked improvement in the character of the skin.

The number of cases under treatment has been small, but includes incipient and advanced pulmonary, also bone and glandular conditions. Though it is much too early to make any radical statements, the results have been so similar to those reported from France that it appears that we have in this isotonic sea water a material aid in the treatment of tuberculosis, especially in the cities and where the patient is forced to work, as in my cases the mode of life has not been changed in any essential. No drugs have been used, with the exception of an occasional gastro-intestinal tonic.

The marked improvement in nervous symptoms and in one case the relief of a distressing dysmenorrhea are worthy of note.

In all the nutritional disorders of infancy and childhood this treatment has proved of distinct benefit, as the digestive power has been much increased. There has been gain in weight in all these cases, in some very marked, while in others it has been slight. Where vomiting, diarrhea, or constipation has been a prominent symptom, it has been improved, and in almost every case cured. The change in the condition of the skin has been most marked. The only other treatment given these cases has been a preliminary evacuation of the gastro-intestinal tract and careful attention to diet.

The use of this treatment in serious cases of pneumonia and typhoid fever has not been frequently enough observed for our deduction to be of great value, but in cases of great respiratory difficulty, with cyanosis and bad pulse, it does have a marked action, evinced in lessened respiratory difficulty, with improvement in the cyanosis and pulse. The same may be said of typhoid fever when the pulse is bad, and also in cases in which there is an intense diarrhea or marked constipation.

In the cases of eczema treated by this method the results obtained were far more satisfactory than I had expected, as the treatment only varied from two to ten injections for a cure. In some cases a carbolized petrolatum or boric acid ointment was used where there was much itching.

The cure of a persistent leg ulcer, while perhaps not important, is striking. The same may be said of the one case of chorea, on which the result was immediate and effective.

TUBERCULOSIS.

	Cases.	Age.	Number of injections.	Number of days under treatment.	Dosage.	Cured.	Improved.	Original weight.	Loss after treatment.	Ultimate gain in weight.	Blood examination.
					c.c.			lbs.	lbs.	lbs.	
Incipient.	1	24 years	24	78	50–120	..	..	112.0	1.0	0.10	
	2	19 years	33	81	50–120	..	..	124.2	..	3.2	
Pulmonary.	3	9 years	33	76	30–50	..	..	45.0	..	4.3	Hemoglobin, (1) 65 per cent., (2) 60 per cent.; white blood corpuscles, (1) 16,000, (2) 15,600; red blood corpuscles, (1) ——, (2) 3,720,000.
	4	35 years	30	73	50–120	..	..	131.0	..	18.0	
Bone.	5	3 years	6	14	15–30	..	Died pneum'nia	23.0	..	0.8	
	6	11 years	8	20	30–45	..	..	55.0	..	1.0	Hemoglobin, (1) 70 per cent., (2) 85 per cent.; white blood corpuscles. (1) 10,800, (2) 11,200, red blood corpuscles; (1) 6,120,000, (2) 6,250,000.

Diseases of Nutrition.

Inanition, bronchitis, syphilis.	7	10 days	3	5	c.c. 15–30							
	8	12 days	6	10	15–30							
	9	5 days	7	10	15–30							
	10	5 days	8	12	15–30							
	11	11 mos.	6	20	15–30	..	..	13.0	..	2.0		
	12	8 years	18	46	15–60	..	..	52.0	..	5.0	Hemoglobin, (1) 85 per cent., (2) ——; white blood corpuscles, (1) ——, (2) ——; red blood corpuscles, (1) 5,350,000; (2) ——.	
Malnutrition	13	8 years	22	87	30–60	..	..	42.0	..	2.5	Hemoglobin, (1) 75 per cent., (2) 85 per cent.; white blood corpuscles, (1) 5200, (2) 14,240, (3) 12,000; red blood corpuscles, (1) 5,130,000, (2) 4,128,000.	
	14	7 years	11	25	20–50	..	..	43.0	..	1.5	Hemoglobin, (1) 95 per cent., (2) 95 per cent.; white blood corpuscles, (1) 9280, (2) 10,320; red blood corpuscles, (1) 5,130,000, (2) 5,190,000.	
	15	14 years	9	16	30–60	..	..	..	..	..	Hemoglobin, (1) 75 per cent., (2) 85 per cent.	
	16	15 mos.	26	88	15–60	..	..	13.9	0.5½	2.13		
Marasmus	17	5 wks.	33	90	15–60	..	..	7.0	..	1.9		

Diseases of the Skin.

Cases.		Age.	Number of injections.	Number of days under treatment.	Dosage.	Cured.	Improved.	Original weight.	Loss after treatment.	Ultimate gain in weight.
					c.c.			lbs.	lbs.	lbs.
Eczema	18	18 mos.	7	13	30					
	19	11 years	4	9	30–60					
	20	1 year	6	10	15–30					
	21	9 mos.	4	8	15–30					
Acne	22	19 years	26	75	50–150					

Special Diseases.

Chorea	23	7 years	10	31	30–60	..	..	49.8	1.8	0.8
Leg ulcer	24	35 years	13	44	40–90					
Diabetes	25	26 years	14	36	50–90	..	..	131.15	1.2	
Typhoid fever	26	3 years	5	12	15–30					

DISCUSSION.

Dr. R. Max Goepp: I became interested in this subject at about the same time Dr. Le Boutillier began his work, but I have not been so fortunate as to have as many suitable cases in which to test the method. The originator, Simon, made rather remarkable claims for his treatment, and I decided that I would try it in a few cases. Those which I selected showed disturbance of nutrition, and either diarrhea or constipation, or indigestion generally. The cases were so few that I could not draw any conclusions, but a few interesting observations were made. In about 15 cases of various conditions almost all the effects noted were purely subjective. In 3 or 4 cases of skin disease there was cessation of itching almost at once. In tuberculous cases there was, according to the patients' statements, less cough and less sputum, but I could determine no increase in weight or other objective signs of improvement. I expect to report more at length on the subject in the near future.

Dr. James E. Talley: There is no question about the advantage of large quantities of water in typhoid fever. It is the custom at the Presbyterian Hospital to have the patient take six ounces of water every two hours in addition to his food. Unfortunately the few cases we had this autumn were admitted about the third week, and though the resident tried the Murphy method in one or more cases, we did so charily.

Dr. Le Boutillier, in closing: The only thing I should like to add in connection with this treatment is that we have not yet had the real test of it which is in the acute gastro-intestinal disorders among children in the summer time. That is the time when it is said to do the most good. We have had marked results in cases of inanition shortly after birth. We have had only 6 such cases, but there has been marked improvement in a short time. Instead of the constant loss of weight there has been gain, and digestion has been improved. I feel that the treatment will do a great deal of good in the summer diarrheas of infants and young children if it is employed properly and conscientiously.

INTESTINAL PERFORATION DURING TYPHOID IN CHILDREN.[1]

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The modern conception of the symptomatology, diagnosis, and treatment of typhoid perforation in general would seem to be firmly based upon the mass of carefully studied material which is now available. Aside, however, from text-book articles, limited series of personal observations, and scattered case reports, there was but little systematic work done on the subject of typhoid perforation in children with respect to treatment by operation, until the appearance of the paper by C. A. Elsberg[2] in 1903. This paper was based upon a study of 25 cases of perforation operated upon in children, all that were available at that time. While the number of cases was small, the deductions which Elsberg was able to draw were of great interest and importance. It has seemed to us worth while to study the cases occurring in children, and reported since 1903, with a view to confirming, if possible, the rather remarkable findings of Elsberg; and, at the same time, to consider briefly those points in the clinical course of typhoid fever in children that have a bearing on the diagnosis of perforation and to compare these with the symptoms commonly observed in adults.

[1] Read March 3, 1909.

[2] Annals of Surgery, 1903, xxxviii.

Frequency. Perforation in children is usually considered to be relatively infrequent. That this is true of infants and very young children is undeniable. Typhoid fever in young children is not often attended by the grave intestinal lesions which are found in older children and adults. Ulcerations of the bowels are few in number and superficial in character, and we find what is commonly spoken of as the "nervous type" of the disease rather than the abdominal type, which becomes the rule as we approach the age of puberty. Hemorrhage and perforation in the earliest years of life are, therefore, very infrequently encountered. It is not until after the age of four or five years that the intestinal lesions become of a character to favor perforation of the bowel, but from this time on the accident becomes of correspondingly greater frequency. We have collected from various sources 2274 cases of typhoid fever in children in which perforation occurred thirty-five times (1.54 per cent.).

In some of the series studied, notably that of Berg,[1] 154 cases with four perforations, or 2.6 per cent., the percentage was higher. Morse[2] collected 284 cases with no perforations. Griffith and Ostheimer,[3] in 302 cases under two and one-half years, found two perforations (0.66 per cent.). Two cases mentioned by Griffith and Ostheimer, which occurred at the ages of twenty and twenty-one months, respectively, are the youngest authentic examples of which we have knowledge.

We find that the percentages of perforation in typhoid fever at all ages vary from 1.5 (Skutesky) to 3.03 (Murchison) and 3.66 (Armstrong). Harte and Ashhurst,[4] in an analysis of 8881 cases, estimate the frequency of perforation at 2.54 per cent. We have collected 4947 cases, with a percentage of perforation of 2.19.

The relative frequency of typhoid perforation in children and adults is somewhat difficult to estimate, as the figures just quoted include cases of all ages; but it may be safely said that while

[1] Deutsch. Archiv f. klin. Med., 1895, vol. liv.
[2] Boston Medical and Surgical Journal, February 20, 1896.
[3] American Journal of the Medical Sciences, November, 1902.
[4] Annals of Surgery, 1904, xxxix.

perforation occurs less frequently in children, the disparity is less than is commonly supposed, the complication being probably slightly more than half as frequent in the junior class.

Age. In collecting cases of perforation in children for study we have fixed the usual age limit of fifteen years; we have analyzed only cases in which operation was performed and perforation proved; we have not considered cases of peritonitis occurring without perforation, nor have we studied cases of perforation of the appendix in which this lesion was manifestly due to a pre-existing or coincident appendicitis not due to typhoid ulceration. Reported since the publication of Elsberg's paper in 1903, we have found 45 cases in subjects fifteen years of age and younger, the exact age being given in 44. These are as follows:

Case I.—Staunton. Med. Press and Circular, 1903, 609.
Case II.—Cotton. Boston Med. and Surg. Jour., 1906, clv, 151.
Case III.—Russell. Montreal Med. Jour., 1903, 584.
Cases IV and V.—Hays. Jour. Amer. Med. Assoc., 1905, 1267.
Case VI.—Anderson. Intercolonial Med. Jour., 1904, 64.
Case VII.—Boyd and Moore. Ibid., 72.
Case VIII.—Waring. Trans. Clin. Soc., London, xxxvi, 110.
Case IX.—Bowlby. Ibid., 124.
Cases X and XI.—Griffith. Amer. Jour. Med. Sci., 1905, cxxx.
Case XII.—Meakins. Montreal Med. Jour., 1905, 741.
Case XIII.—Harte. Annals of Surgery, 1903, 63.
Cases XIV and XV.—Greaves. Brit. Med. Jour., 1906, i, 373.
Case XVI.—Daniell. Lancet, 1908, i, 1043.
Cases XVII and XVIII.—Butler. Jour. Amer. Med. Assoc., November 11, 1905, 1468.
Case XIX.—Vickery and Cobb. Boston Med. and Surg. Jour., February 7, 1907, 177.
Cases XX and XXI.—Manges. Jour. Amer. Med. Assoc., April 1, 1905, 1023.
Cases XXII, XXIII, and XXIV.—Scott. Univ. Penna. Med. Bull., May and June, 1905.
Case XXV.—Bichat. Rev. méd. de l'est., 1904, xxxvi, 431.
Case XXVI.—Scott. Univ. Penna. Med. Bull., May and June, 1905.
Case XXVII.—Stewart. Amer. Jour. Med. Sci., May, 1904.
Cases XXVIII and XXIX.—Scott. Ibid.
Case XXX.—Stewart. Ibid.
Case XXXI.—Maclean. Canada Lancet, 1904, xxxvii, 1011.
Case XXXII.—Griffith. Unpublished, Univ. Hosp. Histories.
Case XXXIII.—Jopson. Archiv. Pediat., March, 1904.
Case XXXIV.—Kaehler. Deut. med. Woch., 1907, No. 34, 1370.
Case XXXV.—Turner. Australasian Med. Gaz., 1904, No. 28, 334.
Cases XXXVI and XXXVII.—Griffith and Hutchinson (unpublished). Children's Hospital Histories.
Case XXXVIII.—Morestin. Rev. de chirurgie, April, 1908, 569.
Case XXXIX.—Rath. Harte and Ashhurst's tables, St. Timothy's Hospital Histories.
Case XL.—Glazebrook. Virginia Med. Semimonthly, 498.
Case XLI.—Newell. California State Med. Jour., 1908, vi, 103.
Case XLII.—Jopson and Gittings (unpublished). Presbyterian Hospital Histories.
Case XLIII.—Mauclaire. Bull. et mém. de la soc. de chirurgie, 1908, xxxiv, 449.
Cases XLIV and XLV.—Hays. Penna. State Med. Jour., January, 1908.

The youngest were aged five years, of which there were 4; 2 recovered, and 2 died. There were 3 patients aged fifteen years, all of whom died. The numbers and ages were as follows:

	Years.		Years.
4 cases at	5	2 cases at	11
4 cases at	6	4 cases at	12
2 cases at	7	3 cases at	13
7 cases at	8	5 cases at	14
4 cases at	9	3 cases at	15
6 cases at	10		

Of 21 cases under ten years of age, 12 recovered and 9 died, a mortality of 43 per cent.; of 23 cases ten years of age or over, 10 recovered and 13 died, a mortality of 56.5 per cent.

This shows apparently a less mortality in young children, which is further corroborated by an analysis of Elsberg's table. In his series, of cases under ten years of age, the mortality was 20 per cent.; in cases ten years of age and over the mortality was 46.6 per cent. As we approach the age of fifteen, the mortality approximates that of adult life.

Sex. The sex was given in 43 of our 45 cases: 28 were males and 15 were females, a disparity much less than that observed by Elsberg, of whose cases, 18 were males and 6 females.

Of 3071 cases of typhoid fever in children that we have collected from various sources, 1659 were males and 1412 were females, a proportion of 1.17 males to 1 female.

Of 7848 cases of typhoid fever at all ages gathered from the statistics of Murchison, Curschmann, and others, 4452 were males and 3396 were females, a proportion to 1.31 males to 1 female. Except for Elsberg's and our own figures, we have found none which give the proportion of male to female in regard to the occurrence of perforation in children. Combining our figures with Elsberg's, there are 36 males and 21 females, a proportion of 1.7 males to 1 female.

In adults the preponderance of males over females who have been operated on for perforation is admittedly large. Harte and Ashhurst give the proportions as about 4 to 1; Finney,[1]

[1] Johns Hopkins Hosp. Rep., vol. viii.

3 to 1; and Scott,[1] men and boys, 77; women, 7 (11 to 1). Curschmann[2] considers that this disproportion in adults is not due to any inequality in the development of typhoid ulceration, but probably to the fact that in men convalescence is unfavorably influenced by previous derangements of digestion due to diet and mode of life; that they submit to treatment at a later stage of the disease than women; that they are more impatient and more careless during convalescence. In view of the almost equal proportion of sexes attacked by the disease, the disparity in the number of adult males to females who suffer from perforation might be satisfactorily explained on these grounds, as we find in children, in whom such etiological factors are absent, that the disparity in the sexes is greatly lessened.

Type of the Disease. In 31 cases of our series, the type of the disease previous to perforation was mentioned. Eight were mild, fifteen were moderate, and eight were very severe; of the mild cases, five recovered and three died; of the cases of moderate severity, eight recovered and seven died; of the very severe cases, two recovered and six died. The influence of the severity of the attack upon the prognosis in cases of perforation as shown by these figures seems to be considerable. The child who is toxic and exhausted by prolonged hyperpyrexia is in poor condition to resist the additional complication and operative intervention.

That children, as a rule, suffer from a milder type of the disease than adults is generally admitted; and it is probable that this, in part, explains their lower mortality after perforation. To this rule, of course, there are well recognized exceptions. The age is an important factor. Children under three years of age and over ten years show a much higher comparative mortality, in the former exceeding, and in the latter approaching, that found in adult life. The influence of the severity of the disease upon the occurrence of perforation, however, has not been universally agreed upon. In adults, the majority of recent writers admit

[1] New York Med. Jour., 1907, lxxxv; Univ. Penna. Med. Bull., May and June, 1905.
[2] Nothnagel's Encyclopedia, American edition.

that the severe cases are most prone to the accident of perforation. The most noteworthy exceptions exist in the ambulatory cases, in which the occurrence of perforation is comparatively frequent. Of 68 cases of perforation reported by Finney, 39 were ambulatory, 10 moderately severe, and 19 severe. Only 8 of the 31 cases of our own series, in which the type of the disease was mentioned, were severe.

Time of Perforation. In 44 cases the time of perforation was definitely stated. In the second week there were 11 perforations, the earliest on the ninth day; 6 occurred at the end of the second week (thirteenth or fourteenth day); in the third week there were 12; in the fourth week there were 6; in the fifth week, 3 (one relapse); in the sixth week, 4 (three relapses); in the seventh week, 3 (all relapses); in the eighth week, 1 (a relapse); and in the ninth week, 1 (a relapse). One occurred one month after convalescence. Among the cases that perforated in the second week there were 6 recoveries and 5 deaths; in those perforating in the third week there were 3 recoveries and 9 deaths; in the fourth week, 2 recoveries and 4 deaths; in the fifth week, 1 recovery and 2 deaths; in the sixth week, 3 recoveries and 1 death; in the seventh, 1 recovery and 2 deaths. The cases perforating in the eighth and ninth weeks and one month after convalescence all recovered. If these figures prove anything, it is that the severity of the disease, rather than its protracted course, contributes toward its mortality. The danger of perforation is greatest at the end of the second and during the third week—42.8 per cent. of all cases occurring during this period. This proportion corresponds rather closely with that of Elsberg (10 out of 24 in the third week). In adults also perforation occurs most frequently during the second and third weeks.

Relapses. Of our cases, 9 were in relapse at the time of perforation; in another, a probable relapse, the duration of the disease was not stated, thus making 10 cases in all. The date of the perforation ranged from the seventh to the fifteenth day of the relapse. Of these cases, 6 recovered and 4 died, a percentage of recoveries higher than that observed in unrelapsed

cases. This, again, seems to confirm the conclusions mentioned above in regard to mortality being influenced by the severity rather than by the duration of the disease.

Harte and Ashhurst found a mortality in 15 cases of relapse of 46.6 per cent.; and in the convalescent cases, 36.6 per cent. – which is much lower than at any stage except in the first week (33.3 per cent.). Their highest mortality was observed in cases perforating in the third week (78.1 per cent.).

Pain. The importance of pain as a symptom of perforation is shown by its occurrence in practically every case of our series of which details were given. In only eight cases, taken from tables, or discussions, in which scanty data were furnished, was it not mentioned; and in one of these the child was under the influence of morphine. It may be considered in its relation to the time of development, its severity, location, and persistence.

In 87.5 per cent. (21 out of 24 cases) it was an initial symptom; in one case it was mentioned as not being initial; in two other cases it had been present during the illness to such an extent as to constitute a difficulty in diagnosis. In 89 per cent. (25 out of 28) the pain was severe. In the remaining 11 per cent. it was stated to be not severe. In 58.6 per cent. (17 out of 29) the pain was general in distribution. In 24.1 per cent. (7 out of 29) it was confined to the right side of the abdomen, especially the right iliac region. In 10 per cent. (3 out of 29) it was noted in the left side. In one case it was noted in the "upper," and once in the "lower," abdomen. In 10 out of 17 cases the pain was persistent, in four of which it continued to increase in severity. In 3 out of 17 it was intermittent in type; and in 4 it was distinctly stated to be "not persistent." In practically all of Elsberg's cases pain was the initial abdominal symptom. It was usually localized to the lower abdomen, especially the right side, and was generally paroxysmal; in a few cases it was constant.

Pain is thus seen to be a very characteristic and important symptom. In the great majority of cases it is an initial symptom and of marked severity. It is more often generalized than local, although it favors the right side in a considerable percentage

of cases, and it is usually persistent, often increasing as time advances.

In Scott's statistics, pain at the time of perforation was observed in 75 per cent. of the cases. Other authors state that it is usually present, but may be entirely absent, although practically all agree in placing it with tenderness and rigidity as one of the three cardinal symptoms.

Except in a phlegmatic, delirious, or semicomatose patient, whether child or adult, the occurrence of pain seems to be almost a *sine qua non*, either of the perforation itself or of the beginning of the localized peritonitis. In such cases it would precede the rigidity, and possibly even the tenderness; and it might even appear to be for a time, at least, an isolated symptom. It would seem to be of great importance to determine the frequency with which sharp pain, not connected with perforation, occurs during typhoid fever.

In the case of children, Adams[1] found it to be an "infrequent" symptom throughout the course of the uncomplicated disease. Edwards[2] found it in 10 per cent. of his cases under ten years of age; and in 40 per cent. between ten and fifteen years. Butler[3] found it in 22.4 per cent. Hand and Gittings[4] record pain or tenderness in 37 per cent. Barthez and Sanne[5] "believe that pain in children is commonly seen in connection with diarrhea, but is usually a transient symptom." Biedert and Fischl[6] also believe that pain and meteorism are neither frequent nor severe in children. In the well-known statistics of McCrea[7] pain was found in about one-third of 500 adult cases at some time during the course of typhoid fever. It was most constantly present with perforation and was closely simulated in cases of hemorrhage, phlebitis, and in some cases of unknown origin. In two-fifths of all the cases of pain, no adequate cause for it was found, and in 14 per cent. the pain was due to some condition other than

[1] Archiv. Pediat., February, 1904.
[2] Ibid., September, 1907.
[3] Jour. Amer. Med. Assoc., 1905, xlv.
[4] Archiv. Pediat., June, 1906.
[5] Rev. des malad. des enfants, third ed.
[6] Lehrbuch. der Kinderkrankheiten, twelfth ed.
[7] New York Med. Jour., May 4, 1901.

the intestinal lesions. Shattuck, Warren, and Cobb[1] found a record of pain in only 5 out of 70 cases without perforation or peritonitis.

While the figures of various observers both of cases in childhood and adult life vary from 7 per cent. to 37 per cent., it is, nevertheless, apparent that a real difficulty in interpreting the symptom of pain will often exist. That its occurrence can never be safely disregarded is equally obvious. The various conditions which, by giving rise to pain, may simulate perforation will be considered under the heading of diagnosis.

Tenderness. Tenderness was noted as being present in 36 out of 45 of our cases. Its absence in the others may depend largely on insufficient data. It was recorded as "general" in 15 cases; prominent in the right iliac fossa in 9; confined to the "lower abdomen" in 2; and once to the hypogastrium.

A study in regard to the time of its occurrence showed its presence both in the early and in the late stages. In only one case was it absent "early," and in this one it developed later. Elsberg found tenderness in every case studied, and in six cases it was most marked in the right iliac fossa. He emphasizes the interval of time which occurs between the development of pain and the appearance of tenderness. As has been said, tenderness forms one of the tripod of cardinal symptoms, upon which the majority of observers rest the diagnosis in adults, although its absence in rare cases has been noted by competent observers.

Rigidity. Rigidity may be regarded as another important diagnostic symptom. It is almost invariably present. It was noted as being absent in only 1 of 32 cases of our series in which full data were given; and in one it was absent early but appeared later. Elsberg found it more or less marked in 14 cases. Its late appearance often depends upon general peritonitis; but when found early, it becomes, in children, as in adults, a most valuable aid to diagnosis.

Vomiting. In 26 cases, vomiting was present twenty times and absent six times. Of the 20 cases, it occurred as an initial

[1] Boston Med. and Surg. Jour., June 21, 1900.

symptom in 4; and in 4 others it was noted within four hours of perforation. In a large number of cases in which it was not mentioned it was probably absent; and in the positive cases it must often be a symptom of peritonitis rather than of perforation itself. Elsberg found it present early in four cases, occurring more frequently as the case progressed, but sometimes absent even in the presence of advanced peritonitis. In adults, Finney found vomiting with perforation in 26 of 68 cases. It will be seen, therefore, that, while vomiting is frequent and a symptom of some value always to be inquired for, it cannot be considered as characteristic.

Distention. Distention was noted as being present in 19 cases and absent in 11. In 9 early cases (within six hours of perforation) it was present in 3 and absent in 6, while in 21 late cases (after six hours) it was present in 16 and absent in 5. In the other cases it was not recorded.

Distention was present in only 50 per cent. of the cases that recovered and in 91 per cent. of the cases that died. Some degree of distention was observed in 19 out of 22 cases in Elsberg's tables, although in only 10 was it of more than moderate degree. As one explanation of its early occurrence, it must be noted that distention is often present in an uncomplicated case of typhoid during the second or third week; while its frequency as a late symptom, taken in connection with its presence in so large a proportion of the fatal cases, simply indicates its significance as a symptom of peritonitis. Of 749 cases of typhoid fever in children collected by Morse, Adams, and Hand and Gittings, 209 (26.5 per cent.) showed the presence of distention during the course of the disease, apart from the complication of perforation. Curschmann believes that, while distention is more common in children than in adults, it is generally more moderate in degree in the former than in the latter. Distention, therefore, seems to be of scant value in the early diagnosis of perforation in either children or adults.

Liver Dulness. In 16 cases the normal area of liver dulness was diminished or almost obliterated; five times this was noted

in early cases. Elsberg noted it in only 5 cases, and emphasizes the fact that distention alone may cause a diminution in the normal area of dulness. Its value as a diagnostic sign is certainly greatly lessened by this fact. In adults Finney found obliteration of hepatic dulness in only 5 of 68 cases, and Shattuck, Warren, and Cobb in only 2 of 24 cases. Harte and Ashhurst consider it a most unreliable symptom. Diminution of liver dulness thus will rarely give material aid in the early diagnosis of perforation.

Effusion. Effusion, as indicated by movable dulness in one or both flanks, was noted as being present in 8 of our cases. The failure to record it may be explained partly by the difficulty often experienced in determining the presence of small amounts of fluid, and partly by the impossibility of distinguishing between fluid within the bowel or free in the peritoneal cavity, without movement of the patient to his side, a procedure which is manifestly attended with risk of spreading the peritoneal infection. The absolute determination of a rapidly increasing movable dulness in the flanks which were previously tympanitic is of undoubted value in corroborating a diagnosis, but will rarely be available for establishing it. Other abdominal symptoms not noted in our cases demand attention. Curschmann refers to the condition of paralytic ileus and consequent constipation, which is apt to develop soon after perforation. While this would seem to depend upon a rapidly spreading infection of the peritoneum, yet it may be noted some hours before the patient's case has reached a surgically hopeless condition. Taylor[1] considers that inhibition of peristalsis forms one of the most important symptoms of the perforative accident. In very few of the case records which we have consulted was the presence or absence of peristaltic sounds noted. More careful attention to this point might furnish valuable aid to diagnosis.

Temperature. In 12 cases information as to the temperature was entirely wanting. In 10 cases the temperature was given at varying times subsequent to perforation, but without statement

[1] New York Med. Jour., February 1, 1902.

as to its height before perforation. In 7 of these 10 cases it varied from 100° to 103.8° F. In the remaining 3 cases it was "subnormal." In 6 cases it was stated that there was no change in the temperature curve at the time of perforation. In 5 cases there was a distinct rise varying from 1° to 5°. In 11 cases there was an immediate drop; this averaged from 3° to 4°, one of 7° and another of 10° being recorded. In one case there was a late drop of 6°. Analyzing these figures, we find that of 33 cases there were 15 in which the temperature was depressed at some time subsequent to perforation, and that in 11 of these it was specified that there was an immediate drop. In 6 cases it was definitely stated that there was no change. In 5 cases it was stated that there was a rise at the time of, or shortly after, perforation; and in 7 cases the temperature given, presumably at the time the diagnosis was made, was fairly high. In these there may have been a slight drop, or one more pronounced with a subsequent rise. In only 33 per cent. of the cases was it specifically stated that there was a pronounced initial drop in temperature; so that, while this is suggestive of perforation, it is probably absent in more than half the cases occurring in childhood.

We are more inclined than Elsberg to lay stress on an initial drop as a feature of significance in diagnosis. He found it recorded in only 4 of his 25 cases. It must not be forgotten that a drop in temperature may be a symptom of intestinal hemorrhage with or without perforation. In 2 of these 4 cases of Elsberg both hemorrhage and perforation were associated with the fall of temperature.

When we compare the conditions found in adults, we find authorities differing as to the frequency of this initial drop. Finney found it recorded in 14 of 68 cases. Harte and Ashhurst consider it significant but not diagnostic, while Harte,[1] in another communication, considers that a fall in temperature associated with sweating is a fairly constant accompaniment of perforation. The necessity for recording the temperature promptly after the

[1] Boston Med. and Surg. Jour., July 18, 1907.

first symptoms is obvious, as the subsequent rise may occur so rapidly as to mask the initial fall.

Chill. The interesting observation of a chill at the time of perforation was recorded in 6 cases of our series. In view of the rarity of chills during an uncomplicated attack of typhoid in children, their occurrence during the second or third week should lead to careful examination of the patient for other symptoms of impending or existing perforation.

In adults, Scott found that in 16.9 per cent. of his cases the occurrence of perforation was marked by a chill. Harte considers a chill infrequent, and Curschmann says that it occurs occasionally, especially in those cases with subsequent elevation of temperature.

Pulse. In 34 cases more or less satisfactory observations upon the pulse rate were furnished. In 8 there was no material change; in 8 there was an average rise of 39 beats per minute, the increase ranging from 12 to 70; in 9 cases the pulse was rapid when they came under observation, the rate ranging from 140 upward. In others it was simply described as weak, rapid, or running. This condition was sometimes explained by an advanced peritonitis, but more often by initial shock. In 4 cases the rate varied only from 112 to 124; presumably in these cases the pulse showed no change. In 2 cases a slight slowing of the pulse was subsequently recorded, probably after an initial rise. Elsberg found decided change in the pulse in 15 cases; the rate increased and the quality diminished. In 5 cases this change was a sudden and early one. The majority of cases, therefore, in children, as in adults, show an increase in the rapidity of the pulse rate; and in a considerable number, a weakening in the quality of the pulse may be looked for as an accompaniment of intestinal perforation.

All writers seem to lay stress on the quickening of the pulse in adults after perforation. Harte and Ashhurst found a rise within fifteen or twenty minutes in the vast majority of cases. Briggs considers the change of pulse of the greatest importance, and Curschmann states that it may be the first indication of the grave significance of abdominal pain of sudden onset.

Shock and Facies. Does shock occur as an early symptom of perforation in children? Elsberg believes that they "seldom show the sudden symptoms of collapse that are so frequent in adults." The results we have obtained in our studies are not in accordance with this view. Shock was distinctly stated to be a marked symptom in 10 out of 45 cases, the most prominent alteration being in pulse and facies, and sometimes temperature — a rapid increase in the first; a pinched, pale, anxious expression in the second; and a fall in temperature, being the concomitant features. In 3 cases in which there was no shock the facies showed no change. In this connection we may mention the facies which is found in cases of advanced peritonitis, the well-known Hippocratic type. In 12 out of 14 cases of perforation observed late (after six hours) this appearance was noted. Curschmann considers that the change in facial expression corresponds approximately with the local manifestations.

Taken in connection with the change in pulse and temperature change in facies assumes some importance; but alone, it is doubtful whether it could be satisfactorily interpreted.

Respiration. The study of the data on respiration was unsatisfactory. Change in the rate is probably not of very great moment. In 5 cases, some seen early and some seen late after perforation, absence of abdominal respiration was noted—a symptom which is not often looked for, or, at least, recorded, but one which we think is probably of some importance. In 2 cases it was stated that abdominal respiration was present. In only 7 of the 45 cases, therefore, are any records available. We would emphasize the necessity of more careful observation on this point.

Leukocytosis. Leukocytic counts were recorded in only 14 cases in our series; in 6 of these repeated observations were made. In 2 of these 6 cases an increase of from 2000 to 3000 leukocytes was observed after perforation, both cases ending fatally. In two others which recovered a rise respectively of 2000 and 7000 was found. In the remaining 2, both of which were fatal, a falling count was recorded, which is in accordance

with what has been observed by other writers, namely, that the outpouring of leukocytes in the effusion of peritonitis seems to act, at times, as a depleting agent to the circulation. Of the single counts taken within a few hours of perforation, 3 were under 8000. Of these cases, 2 recovered and 1 died. Of the cases showing counts of 10,900 and 12,440 respectively, one recovered and one died; while of the three which showed a count in excess of 18,000 all recovered.

The number of these cases is too small to permit of conclusions being drawn, but they suggest that a falling count is unfavorable, while a high count or a rapidly rising count is of better prognostic significance. Elsberg found a sudden or gradual rise in 5 cases, and believes that frequent counts in the early stages may be of confirmatory value, but even here may lead the surgeon astray. We may conclude, therefore, that leukocytosis often accompanies the accident of perforation in children; and without being an infallible sign, yet it forms one of the features in the symptom complex. The attempt to establish a normal average of leukocytes throughout an uncomplicated attack of typhoid in childhood is difficult. Hand and Gittings found counts in 71 cases, which ranged from 5000 to 10,000; while 31 cases gave counts varying from 10,000 to 16,000. All of these occurred in uncomplicated cases.

Many authors, in writing of typhoid fever in the adult, are inclined to attach little importance to the leukocytic count in relation to perforation, owing largely to the wide range found in uncomplicated cases; others consider that the subject needs further study before any conclusion can be drawn. Shattuck, Warren and Cobb, Cushing,[1] Thayer,[2] and others attach much importance to a rise shown by hourly estimations.

Blood Pressure. The question of blood pressure at the time of perforation has recently received attention, but we have found no records of estimations in children. In adults results so far recorded show a distinct rise within two hours of perforation. After this time the pressure falls.

[1] Johns Hopkins Hospital Reports, viii. [2] Ibid.

Duration of Perforation before Operation. There were 10 cases which were operated upon within six hours of perforation, of which 7 recovered and 3 died; of 10 cases operated on between six and twelve hours, 5 recovered and 5 died; of 8 cases operated on between twelve and twenty-four hours, 3 recovered and 5 died. Between twenty-four and forty-eight hours there were 8 cases, of which 3 recovered and 5 died. After forty-eight hours there were 2 recoveries and 1 death.

There is here evident a steadily rising mortality after six hours. The recoveries in 2 of the late cases can be explained only on the theory of personal resistance to infection, lessened virulence of the intestinal bacteria, or more probably to partial localization of the infecting material. The same observation is made in late cases by Harte and Ashhurst.

Elsberg's figures show 100 per cent. of operative recoveries in the first eight hours, and 86.6 per cent. of recoveries in the first sixteen hours. After this time only 44.4 per cent. of recoveries are noted. All statistics confirm the value of early operation. The third hour was the most favorable period according to Harte and Ashhurst's tables; and after this a rising mortality was observed.

Description of Perforation. *Number.* In 3 of our fatal cases there was a double perforation at the time of operation, in one of which one of the perforations was overlooked and discovered at autopsy. In a fourth case there were two perforations in the ileum and two in the appendix. This case recovered. In 8.9 per cent. of the cases, therefore, the perforations were multiple at the time of operation. Comparing with adults, we find that 12.5 per cent. of Harte and Ashhurst's cases showed multiple perforations.

Situation. In our cases of single perforations the site in 20 cases was within twelve inches and in 5 cases within two feet of the ileocecal valve. In 2 cases the notes record it "within a short distance," and in one case in the appendix; 81.5 per cent. of the cases, therefore, were in the ileum within a foot of its termination. In adults, Harte and Ashhurst found that in

73 per cent. the perforation occurred within twelve inches of the ileocecal valve.

Size. Nineteen of the perforations in our cases were of small size (pin point, one-sixteenth to one-tenth inches), and 10 were large.

Secondary Perforation. Three cases of secondary perforations were recorded in our series, all of which were fatal; of these, one was in the jejunum. This gives a percentage of 6.6 per cent. of secondary perforations. In Elsberg's series there were four instances of multiple perforation, and of these, probably two, and possibly three, were secondary. This is interesting when it is noted that in Harte and Ashhurst's 362 cases there were only 12, or 3.3 per cent., of secondary perforation.

Complications. There were 3 cases of secondary perforation after operation. One had hemorrhages on the second and fifth days after operation; a second case had pleurisy, bronchopneumonia, and a fecal fistula. Another case, already mentioned, died of an undiscovered perforation, which was present at the time of operation. There were four other cases of fecal fistula developing after operation, all of which recovered, as did 2 cases of Elsberg's. These are of interest in connection with the observations of Hays[1] and others who have commented on the favorable course of cases developing fecal fistula after operation.

In the first 10 recoveries in Hays' practice there were 5 cases of fecal fistula, and in 16 similar cases of Harte and Ashhurst's series the mortality was only 12.5 per cent. There were two fatal cases of suppurating parotid bubo, one of which was bilateral, and 3 cases in which secondary abscess in the abdominal cavity developed, 2 of which were fatal. The latter were probably due to deficient drainage or unavoidable pocketing of infected collections of fluid. Two cases of postoperative intestinal hemorrhage were recorded, one of which recovered. In another case (authors') there was a hernia of several loops of bowel from the wound, following the removal of loose gauze drainage five days

[1] Jour. Amer. Med. Assoc., 1905, 1267; Penna. Med. Jour., January, 1908.

after operation. Etherization was required for its reduction. We know of another case in an adult in which this accident occurred; caution should be exercised in the removal of gauze, for this reason. There does not seem to be a tendency for the formation of extensive adhesions in these cases when we consider that only 3 deaths out of 89 in Harte and Ashhurst's series were due to subsequent intestinal obstruction; no example of this sequel occurred in our own series and only one in Elsberg's.

Analysis of Deaths. In our series there were 23 recoveries and 22 deaths, a mortality of 48.8 per cent. In Elsberg's 25 cases there were 16 recoveries and 9 deaths, a mortality of 36 per cent. Combining these figures, we find a total mortality in children of 44.28 per cent. The average mortality in adults as given by various authors equals about 75 per cent. It remains to consider fatal cases with respect to the time at which death followed operation. There were no deaths on the table. Eight patients (38 per cent.) died within twenty-four hours after the operation, as contrasted with 36 per cent. for this same period in Harte and Ashhurst's series. Two patients died on the second day and three on the third day. This gives 64.7 per cent. of the total mortality for the first three days, as compared with 76 per cent. for the same period in the Harte and Ashhurst tables. One died on the fourth, one on the fifth, one on the seventh, and one on the eighth day; and four patients lived respectively twelve, fifteen, twenty-three, and thirty-one days after operation. In these late cases death was due to secondary perforation, pneumonia, parotid bubo, secondary abscess, etc., some cases showing multiple complications. Of the three cases of secondary perforation, death occurred on the fourth, eighth, and twelfth days respectively.

Diagnosis. The important diagnostic symptoms which are shown by a study of our cases are pain, tenderness, and rigidity, which in children, as in adults, are early in their development and fairly constant in appearance. Next in importance, because less frequent, but of significance when present, are a drop in the temperature, a rise in the pulse rate, and some degree of shock,

often preceded or accompanied by vomiting, with perhaps a preceding or accompanying chill. A wave of leukocytosis will sometimes be recorded, and is at least as significant, if not more so, than in adults. Distention, and obliteration or diminution of liver dulness are of little value in making the diagnosis in children, while effusion is mainly of value in confirming it. Other points are an absence of abdominal respiration, inhibition of peristalsis, and possibly a rise of blood pressure, hitherto unstudied in early life. The accident of perforation may be simulated in children, as in adults, by a number of other conditions.

Appendicitis. We have operated for acute perforative appendicitis in typhoid fever in a child under the diagnosis of perforation. The diagnosis between the two may usually be made from the fact that in appendicitis in typhoid fever, while the local symptoms are the same, their development is not usually marked by the same degree of constitutional involvement in the way of shock, fall of temperature, and rapid rise of pulse rate as in perforation; nor is the course toward a fatal issue so rapid, if operation is not done. We have seen a case, in the service of a colleague (Hodge), of peritonitis without perforation, in a child who recovered from the operation. Such a case would be difficult or impossible of diagnosis from perforation, and operation would be equally indicated.

Hemorrhage. This may simulate perforation, or may precede or follow it. When pain is not present, it will not be difficult to distinguish. When pain and collapse are present before the appearance of blood in the stools, local and general symptoms must be carefully studied. The occurrence of previous hemorrhage would put the physician on his guard. The absence of rigidity and marked tenderness, and of leukocytosis, vomiting, and chill, are points in favor of hemorrhage.

Retention of Urine. While we know of no cases in childhood in which a distended bladder has caused pain suggestive of perforation, the occurrence of this condition is as easily conceivable, or more so, than in the adult, in whom it has to be reckoned with as a source of possible error in diagnosis.

Pneumonia and Pleurisy. A right-sided pleurisy or pneumonia very frequently simulates an inflammatory process in the right iliac fossa in childhood; examination of the base of the chest posteriorly should invariably be made when pain and rigidity are observed in the right side of the abdomen.

Flatus and Intestinal Colic. The local and constitutional symptoms of an inflammatory process will usually be wanting.

Rarer affections, perhaps simulating perforation, such as suppuration of mesenteric glands, intestinal obstruction of mechanical origin, intussusception, venous thrombosis, etc., need only be mentioned in this connection. Finally, it may be assumed that the accident of perforation is quite as likely to be overlooked in children as in adults. The difficulty in eliciting the symptoms in young children, both objective and subjective, is the greatest stumbling block in the making of a diagnosis.

The Technique of Operation. It remains to analyze our statistics with regard to the technique employed. In the large majority of the cases the usual right iliac incision was employed. There is little difference in opinion as to its merits and the preference to be shown it. In three cases, probably on account of the condition of the patient, local anesthesia was employed. All of these cases ended fatally. While local anesthetics have undoubted advantages at times in adults, and are used practically as a routine by some operators (Hays), their employment in the young is open to serious objection on account of the excitability of children and the difficulty in controlling them. Elsberg prefers chloroform anesthesia in children, but our own preference is for ether. In two cases the appendix was removed for perforation. There are no special data in our tables as to the type of sutures used to close the perforation. A double row of interrupted Lembert sutures, applied in a direction longitudinal to the bowel, is usually sufficient. A purse-string suture, for a small perforation, reinforced, if necessary, and omental grafting, to reinforce the sutures, for larger perforations may be used. As Elsberg points out, primary resection of the bowel in cases with a very large ulcer should never be done, if it is possible to avoid it. Indeed,

we question whether it should ever be considered in children. When a perforation is too large to suture without the danger of occluding the lumen of the bowel, it will be far better to establish an artificial anus at once by primary enterostomy.

Primary Enterostomy. The favorable influence of the development of a fecal fistula upon the prognosis, and the arguments based thereupon in favor of primary enterostomy instead of suture of the perforation at the time of operation, have been touched upon in the consideration of complications. Hays recommends enterostomy as a routine measure. Two cases in our series in which an artificial anus was established died. Without doubt, enterostomy is an operation which is growing in favor, both for obstruction and for peritonitis.

The question of its routine employment may still be considered an open one. The near future will determine whether its disadvantages are offset by a decrease in mortality when it is adopted. We are heartily in favor of anchoring the sutured segment of the bowel in the wound, which was done in two of our cases, with favorable issue.

Treatment of Effusion. The fluid was removed by irrigation in at least 19 cases in our series, with 11 recoveries; and by wiping or sponging in 6 cases, with 4 recoveries. Surgeons are still divided as to the relative merits of irrigation and non-irrigation in the treatment of abdominal effusions of infectious material. Most of the arguments commonly used against it are valid in the consideration of infections of a different type, especially those of appendicular origin, when the infection is a slowly spreading one from a limited focus, and when a large area of the peritoneum is not involved. In perforations of the bowel of other types, and in gastric perforation, especially from ulcer, when the peritoneum is often flooded with intestinal or gastric contents and inflammatory exudate, we believe irrigation furnishes the quickest and most effective means of removing this infectious material. Evisceration should never be employed in children, whose susceptibility to shock is well known.

Rapidity of operation is even more essential in children than

in adults, on account of the danger of fatal shock. Our experience in operations upon children leads us to indorse the opinion of Elsberg that children bear abdominal and other operations well, if manipulations are not prolonged. Moreover, their recuperating powers after operation are greater than adults, and the reaction is more rapid and more complete.

Drainage. At least three cases were closed without drainage of the abdomen; and of these, two recovered. Tube or tube and gauze were used in the majority of cases, in which the character of the drainage was described. Since the widespread adoption of the principles of the Murphy treatment of diffuse peritonitis, we hear less about leaving infectious collections to the tender mercy of the peritoneum. A tube in the pelvis for existing or potential collections can do no harm, and a gauze strip to the region of the sutured ulcer, unless the bowel be anchored in the wound, is a wise precautionary measure.

Position after Operation. The Fowler position, either alone or in combination with continuous enteroclysis (Murphy), was occasionally mentioned as being practised, and was probably more frequently used. Its advantages are manifest. Nevertheless, the warning sounded by J. Alison Scott as to the wisdom of always employing it is to be borne in mind. He believes it to be occasionally harmful in typhoid cases, and in exhausted or delirious children it may well be found at times inexpedient. Unless contra-indicated by these conditions, however, we would advise it, as we have used it and seen it used to advantage.

In children we cannot withhold either water or nourishment from the stomach as long as we can in adults; nor is it necessary, in the majority of instances, to do so. If the continuous enteroclysis is employed, the patient will suffer less from thirst. After six or eight hours, if there is no vomiting, we see no objection to administering small amounts of water by the mouth; and after twenty-four hours we may begin the administration of albumin water and pasteurized milk by the mouth.

Conclusions. Typhoid perforation is very rare under five years of age; after this period it is not infrequent, being about

half as common as in adults. The favorite time of perforation is at the end of the second and during the third week. The diagnostic symptoms, in the order of their importance, are pain, tenderness, rigidity, fall in temperature, rise in pulse rate and collapse, vomiting, chill, and rising leukocytosis. The mortality after operation is influenced by the severity of the disease rather than by the protracted course. It is lower under ten years of age than after this time. The mortality is lower in relapsed than in unrelapsed cases. The average mortality is somewhat less than 50 per cent. and at least 25 per cent. lower than in adults. The earlier the operation is performed, the better the prognosis. The technique of the operation does not differ materially from that advisable in adults, except in the use of a general anesthetic and the even greater necessity for rapidity in operation and avoidance of meddlesome surgery.

DISCUSSION.

Dr. J. P. Crozer Griffith: I have been fortunate, or unfortunate in having seen an unusually large number of perforations in typhoid fever in children. I have notes of nine cases. I think there is a tenth, notes of which I have not been able to find. The thing which impresses me most is the extreme difficulty of making a diagnosis early enough to admit of operation being of any value to the child. Four of the cases, as I recall it, were operated upon. In one or two of the others the operation could not be done for reasons into which I need not enter. In at least two the diagnosis was not made, the symptoms being absolutely deceptive. In one instance the patient was a little fellow, aged four years, who sat up in bed all of the last day of his life, with no severe pain and no fall of temperature. It was not until shortly before death that he failed rapidly, and perforation was not even suspected until autopsy showed it. In another instance the patient vomited after eating ice-cream, but it was thought simply that the ice-cream did not agree with him. It was not until fully twenty-four hours afterward that perforation was thought of in this case.

I am convinced, so far as my own experience goes, that the disease does not show the characteristic symptoms which we expect to find in adult life. We know, of course, perfectly well that adults, too, may show very anomalous symptoms which do not lead to a suspicion of the complication. But my belief is that in children this is more often the rule than the exception. Some

little time ago I had occasion to look over the temperature charts of the nine cases of which I have spoken, in the attempt to find one which might be called typical, but none of them were suitable. If any drop in temperature had occurred it was in the three-hour intervals between the making of observations. There was, it is true, the later rise of temperature which occurs after it is too late to have operation do any good. Children as well as adults have abdominal distention in typhoid fever, and it is often very difficult to determine whether this is due to gas within the bowel or outside of it. The same remark applies even with greater force to the question of abdominal pain to which patients with distention are subject. There is even more difficulty in the case of the children, because of the inability to depend much upon what they tell you. An adult can often give you a clear idea of how much pain there is, and how and when it came on; a child, no matter in what good condition his mental state may be, can give no satisfactory information.

Dr. J. Alison Scott: Personally I am very much indebted to Drs. Gittings and Jopson for their most excellent paper. I have for a good many years been interested in the subject of perforation at the Pennsylvania Hospital, and in the last six months I have tabulated 105 cases which have occurred since May, 1901. Of these cases, only 81 have been operated upon. There is sometimes the tendency to postpone operation in the hope that if perforation does occur it will be plugged by some fortuitous chance. Records, however, show that nature seldom plugs the perforations either by adhesions or omentum, so the hope of a cure being thus effected might as well be given up. We have two very interesting specimens where perforations have been closed. In both instances the adhesions occurred between the ileum and the right posterior surface of the bladder. In both cases the men died from secondary causes, not from the perforation. In one case I recall that there was an abscess of the lung. Peritonitis was not actively present in either case.

In adults statistics show that at least 12 per cent. are undiagnosticated, and I say this with due deference to the skill of the able medical staff of the Pennsylvania Hospital. A very considerable percentage of these are diagnosticated on the autopsy table, and not even suspected during life. The toxic cases were watched with great care, and no symptoms were shown of pain or of peritonitis. I think we must agree that if the diagnosis is more difficult in children than in adults a good many of the cases must be overlooked.

I should like to have Dr. Gittings' opinion upon the association of perforation with hemorrhage. I have seen the abdomen opened with the idea of stopping the hemorrhage and perforation found. The hemorrhagic cases at times are very painful, and will give you many of the same symptoms observed in perforation. If investigations can be carried out in the proper way, I believe that we may be able to localize the ulcers from which the hemor-

rhage occurs. It seems reasonable to think that it occurs from the same ulcers as does the perforation. Almost no postmortem examinations have shown definitely where hemorrhage in typhoid occurs. I believe it would be a step in advance in those cases in which hemorrhage is excessive to permit a surgeon to open the abdomen and hunt for the trouble.

Dr. Gittings, closing on his part: We found no instances of coincident hemorrhage and perforation, but in two cases hemorrhage occurred subsequently, one of which died. The difficulty of diagnosis may, perhaps, not be sufficiently emphasized in our paper, since we have selected only the operative cases in going over the whole study of perforation. The difficulties are great and well recognized. It seems to me that the only solution at present is a more careful study of cases—not so much by the visiting physician as by the resident physician, who is in constant touch with the patient. I feel sure that in the case of children the first symptoms, at times, are overlooked or not interpreted correctly by him, or realized by the nurse.

The question of blood pressure is attracting some attention. We have not found any series of observations upon children. In adults rapid fall of blood pressure has been observed within a few hours of perforation. As to the question of leukocytosis, the individual count is often of no value, but the rising count is very suggestive.

Dr. Jopson, closing: The lower mortality in children than in adults may be explained on several grounds. An important factor is that children with typhoid fever are not as sick as adults. The disease runs a milder course and the complications are fewer. Another explanation is that the reaction from inflammatory conditions of any type, including peritonitis, is apt to be more rapid and complete after operation than in adults. While children are more susceptible to operative shock, at the same time reaction is more rapid and convalescence more complete. They are also not so apt to develop complications directly or indirectly due to preëxisting organic disease.

A CASE OF APPENDICITIS IN WHICH THE OXYURIS VERMICULARIS WAS FOUND IN THE APPENDIX.[1]

By ASTLEY PASTON COOPER ASHHURST, M.D.

Laura P., a Polish girl, aged fourteen years, was admitted on March 14, 1909, to the Episcopal Hospital, in the service of Dr. G. G. Davis, to whom I am indebted for the privilege of operating and of recording the case. Owing to the patient's ignorance of the English language, it was difficult to obtain an accurate history, but it was learned that she had been ailing for a week or ten days, and that twenty-four hours before admission she had been taken with severe abdominal pain, followed shortly by vomiting. The pain was at first general, but later settled to the region of the appendix. Examination at 9.30 P.M., soon after admission, showed great tenderness with some rigidity over the right iliac region. No mass was present. The temperature was 100.6° F., the pulse 88, and the respirations 34 per minute. The white blood cells numbered 25,000 per c.mm. The diagnosis was acute appendicitis.

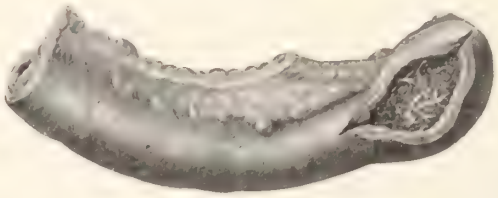
Operation at 10 P.M. Through the transverse incision of G. G. Davis,[2] an appendix was removed which was congested at the tip, but presented no other gross evidences of disease. The abdominal wound was closed without drainage. When the appendix was slit open at its tip, the lumen of the organ was found to contain a number of minute worms, resembling "seat-worms." Subsequent examination under the microscope by Dr. C. Y. White, director of the laboratories of the hospital, confirmed the diagnosis of Oxyuris vermicularis. When warmed up, the worms squirmed around actively. Under the microscope the appendix presented the ordinary picture of acute suppurative appendicitis in the early stage, its walls being studded with miliary abscesses. The patient's convalescence was uneventful, and examination of her feces revealed the presence of many more similar parasites.

My object in reporting this case is to call attention to the fact that the presence of intestinal parasites in the appendix is by no means rare, but that they are seldom, if ever, the direct cause of

[1] Read April 7, 1909.

[2] Annals of Surgery, 1906, xliii, 106.

appendicitis. As I have pointed out in the chapter on the History of Appendicitis, prepared for the third edition (1905) of Dr. John B. Deaver's monograph, Fabricius ab Aquapendente, even as early as 1634, mentions having found at times a worm in the appendix at autopsy; Santorini (1724) made the same observation, and thought that the chief function of the appendix was to serve as a nest for round-worms, where they might be cherished and be prevented from escaping into the general intestinal tract.



Vermiform appendix containing Oxyuris vermicularis. (Natural size.)

Many varieties of parasites have been found in the appendix, especially Ascaris lumbricoides and Oxyuris vermicularis. F. D. Patterson[1] has collected 10 cases in which lumbricoid worms and 8 in which oxyurides were found in connection with diseased appendices. Tape-worm, trichocephalus, echinococcus, and bilharzia disease were also noted in one instance each. To his list of oxyuris should be added 2 cases, reported by Beyea[2] and by Rammstadt.[3]

Still,[4] in 200 consecutive autopsies on children less than twelve years of age, found oxyurides in the intestinal tract in 38 cases (19 per cent.), and of these cases no less than 25, or two-thirds, had the parasites inside the appendix. Oppe, according to Sprengel,[5] found oxyurides six times among sixty appendices removed at operation. Erdman[6] found, among 29 operations for appendicitis in children under ten years of age, 4 cases with oxyurides in the appendix. Rostewsew, cited by Sprengel, found

[1] American Journal of the Medical Science, 1906, cxxxi, 859.
[2] University Medical Magazine, 1900, xiii, 67.
[3] Deut. med. Woch., 1902, xxviii, 919.
[4] British Medical Journal, 1899, i, 898.
[5] Appendicitis, Deutsche Chir., Stuttgart, 1906, S. 182.
[6] New York Medical Journal, 1904, i, 537.

parasites three times in the appendix among 278 autopsies on persons who had not died of appendicitis; and also found them present the same number of times among 163 cases of appendicitis; from which he concluded that their influence in causing appendicitis was trifling.

It is well known that L. Metchnikoff holds parasites responsible for the majority of attacks of appendicitis; and he insists that in every case, before operation is undertaken, a microscopic examination of the feces should be made, and that in cases in which it is possible the effect of vermifuge remedies should be tried, even if this examination is negative. In 1901,[1] when he appears first to have called attention to this matter, he referred to 4 cases in which recurrent attacks of appendicitis ceased after lumbricoid worms had been expelled by the action of vermifuges. He acknowledges that it is not at all probable that the lumbricoids could perforate the appendix or other portion of the intestinal canal, but explains their action on the theory that they first produce erosions of the mucosa, and then deposit in these erosions the microörganisms with which their bodies are covered. In this way, Metchnikoff contends, parasites can be the primary cause of ulceration and perforation of the intestinal wall.

Yet I think the case reported herewith goes to show that even if the worms can be held accountable for the origin of the disease (which is a mere assumption), the lesions in the appendix, even at an early stage, are such as to make prompt operation the safest form of treatment. In this case the walls of the appendix were found on microscopic examination to be studded with miliary abscesses, and it was the opinion of the pathologist that the presence of the worms was a mere coincidence; delay in operation in this, as in most other cases, would have resulted in a localized peritonitis within a comparatively short space of time. From the fact that intestinal parasites are found within the appendix in 12.5 per cent. of children under twelve years of age (Still), it is not logical to conclude that they are on that account frequent causes of appen-

[1] Journal des Praticiens, 1901, xv, 185.

dicitis. It is interesting to note their frequency, and it is important to take measures for their extermination; but the surgeon should not waste valuable time in attempting to cure symptoms of appendicitis by vermifuges, when it is not proved that the worms, even if present, are responsible for the symptoms of disease.

DISCUSSION.

Dr. John B. Deaver: I recall only one case similar to that of Dr. Ashhurst. I believe the presence of the worms was a mere coincidence. In the case I have referred to the appendix was filled with small worms. The appendix had not perforated. Microscopic examination showed much the same condition reported by Dr. Ashhurst. I agree with Dr. Ashhurst that it would be unwise to trust to vermifuges in preference to the treatment which he adopted.

PURULENT MENINGITIS SECOND TO PANSINUSITIS; OPERATION; RECOVERY.[1]

By WM. G. SHIELDS, Jr., M.D., WM. G. SPILLER, M.D.,

AND

EDWARD MARTIN, M.D.

REMARKS BY DR. SHIELDS.

Patient, G. P., aged fourteen years, a well-developed and well-nourished girl, has always been healthy and led an active athletic life, as well as a studious one. Family history negative except that it is good in every respect.

Five years ago developed a right-sided otitis media, which promptly responded to treatment and, with the exception of an acute attack two years ago, has not bothered her since.

Two weeks before the beginning of this illness the patient struck her head with a hanging plant on that portion of the scalp corresponding with the region of the fissure of Rolando on the right side. She did not lose consciousness, and, aside from complicating the diagnosis, the blow was unimportant, as later examination of the shaved scalp and skull showed that this trauma was not a causative factor in the present condition.

I was first called to see the patient on the evening of February 21, 1909, when she had a temperature of 104° F. and a pulse of 124, complaining of general headache and aching pains over the body, with some dull pain in the right upper jaw and right ear, from which there was no discharge and which local examination showed to be apparently normal. There was some slight pharyngeal catarrh and mucopurulent nasal discharge, but the latter had been present for some weeks preceding this time. The heart, lungs, and abdomen were negative. As a sister and brother had recovered from attacks of influenza, in the same house, just preceding this illness, the patient was treated for an influenzal infection.

On February 22 the temperature came down to 102.8° F. and pulse 120, but patient seemed to experience no relief from the general aching pain, and

[1] Read April 7, 1909.

in addition had more severe headache, which was confined to the frontal and temporal regions of both sides. An edema of the right upper lid developed that afternoon and gradually increased until she could barely separate the lids sufficiently to show any of the eyeball. There was no rigidity of the muscles of the neck. The pupils were equal and slightly contracted, but reacted to light and in accommodation.

On February 23 the edema of the right eyelid increased and the lid was purplish in color. The headache was mostly frontal, and there was considerable tenderness at the inner canthus of the right eye, with slight supraorbital tenderness of the right side. The temperature ranged between 103° and 104° F., and pulse 116 to 124, until 5 P.M., when temperature rose to 105.2° F., and patient became very restless. Two hours later she developed a convulsion, commencing with twitching of the lips and rapidly becoming absolutely general, accompanied by opisthotonos, rapid, stertorous respiration, cyanosis, rapid, small, irregular pulse, and biting of the tongue. It lasted for seven minutes, and patient remained in stupor for over an hour afterward. For some hours after regaining consciousness she complained of headache, and seemed confused and drowsy. As has been stated, the temperature remained high during the early part of the illness and did not respond in the least to repeated sponging. The nasal discharge having somewhat lessened, the edema of the right upper lid persisting, and tenderness over the region of the right frontal sinus having increased during the night, together with persistent hyperpyrexia, Dr. Hearst was asked to examine the accessory sinuses of the nose, and found a right frontal sinusitis, which seemed to be draining quite well. Fourteen hours after the first convulsion the patient developed another of exactly the same character, only lasting slightly longer. She was removed to the Germantown Hospital, with a view to the probable necessity of opening the frontal sinus. At this time it was thought that the convulsive seizures were probably due to the hyperpyrexia and toxemia of the infection, together with an acute nephritis which had developed and was shown by the presence of hyaline and granular casts and albumin. The Widal reaction was negative, and a leukocyte count showed 13,800. Culture of the nasal discharge showed streptococci. Heart, lung, and abdominal examinations gave negative results. Dr. Hearst and Dr. Bliss, who also saw the case, decided that in view of the free drainage through the nose and improved local appearance, the condition of the right frontal sinus was not serious enough to warrant opening it from without.

There was some intolerance of light and sound, with excessive irritability and restlessness, but no rigidity of the neck. The right upper lid was still edematous, and there seemed to be some ptosis, but as long as there was nothing abnormal with the muscles of the eyeball, it was thought that the edema could account for the ptosis. Patient complained of considerable nausea

at this time. There was increasing pain in the right frontal and temporal regions, which was somewhat relieved by making continuous pressure with the hand over those regions. She complained of extreme weakness, and at times her thoughts were slightly confused. Temperature, 103.4° to 101° F. Pulse, 122 to 92.

On February 27 the left foot was seen to be extended and inverted. It could be flexed by the examiner, and there was no ankle clonus, but patient was unable to flex the foot for herself. No Kernig's sign on either side. Temperature, pulse, and general condition about the same, but she was still more nervous and irritable, with increasing intolerance of light and sound, and insisted on having pressure made continuously over the right frontal and temporal regions.

On February 28 Dr. Spiller saw the patient for the first time, and will describe the results of his subsequent examinations.

REMARKS BY DR. SPILLER.

Notes made February 28 are as follows: The movements of the lower limbs are not made with great force; the right lower limb is moved almost normally. The left lower limb is moved with a fair degree of power at the hip in flexion, but she is almost unable to make the slightest movement of extension of the left leg on the thigh, and has no movement in the left foot. The left foot is drawn inward, but can be straightened by the examiner without difficulty, although the foot will not stay in the normal position. Ankle clonus is persistent on the left side and resembles organic ankle clonus in every particular. The clonus will persist so long as the foot is held flexed on the leg. No ankle clonus on the right side is obtained, and there is no indication of it. The patellar reflexes are about normal, equal on the two sides, possibly a little diminished, certainly not in the least exaggerated. When she is encouraged to make effort to extend the left leg on the thigh she seems to make a little more effort, but it is impossible to get her to appear to try, even by the use of suggestion with the faradic current. The response from the left external popliteal nerve is normal. She said the left hand was not so strong as the right, but the grasp of each hand is fully normal. The biceps and triceps reflexes are normal on each side. Sensations of touch and pain are normal in the lower and upper limbs. She has no involvement of the facial nerves. The tongue is normal, but much coated. She still has pronounced ptosis of the right upper lid, which was attributed to the previous swelling. Irritation of the sole of the left foot repeatedly produced flexion of all the toes, including the big toe, but occasionally the left big toe was extended. No Babinski was obtained on the right side. The condition of the nose and frontal sinuses has improved,

the fever is less, and the child seems better than she was a few days ago. The marked weakness below the knee, as compared to the slight weakness above the knee on the left side, is striking. While the girl could flex the leg on the thigh, she could not in the least extend it. The ankle clonus, with normal patellar reflexes, and usually normal condition of the Babinski reflex, is also striking.

I saw the patient again the following day, at which time her condition had greatly changed. The examination gave the following results:

The lower part of left side of face is distinctly weak. She is unable to draw up the left corner of the mouth in showing the teeth, whereas she draws up the right corner in a normal manner. In attempting to draw up the corners separately, there is no movement of the left corner. She closes the eyelids firmly, but in resisting the opening of the lids by the examiner, she seems to have a little weakness of the left lids. Too much importance must not be placed on this, as it is difficult to get her to make the proper effort. The tongue is protruded straight. There seems to be no distinct stiffness of neck. She complains of great drowsiness and headache. The latter is frontal and bilateral, but inasmuch as she seems to wish her father to place his hand and press more deeply over the right side, it is possibly more right-sided. She is very irritable, evidently having much pain in the head. Last night she had considerable nausea, but no vomiting. She has no dizziness unless the head be raised. The right ptosis is still pronounced.

The left upper limb is completely paralyzed. She is unable to grasp at all with the left hand, and makes no attempt to move this limb. If the limb be placed in an awkward position, she moves it back with the right hand. She is entirely unable to recognize a finger or penknife in the left hand, even when fingers are closed upon the object. She recognizes objects promptly with the right hand. She made several mistakes in distinguishing the point from the head of a pin in the left hand, but made none in the right hand. Sense of position was not tested. The biceps tendon reflex is slightly exaggerated on the left side and normal on the right side. The triceps tendon reflex is about normal on each side.

The left lower limb is completely paralyzed except at the hip. There is some tendency to inward rotation of the feet, especially the left. That of the right is questionable. The patellar tendon reflex is about normal or a little exaggerated on the left side and lost on the right side. Reinforcement was not tested. Ankle clonus is still persistent on the left side. No indication of it on the right side. Babinski reflex is today absolutely typical on the left side. It is not obtained on the right side. Pain and tactile sensations appear to be normal in both lower limbs. There is slight indication of Kernig's sign on the left side.

The condition was evidently a focal lesion of the right motor cortex beginning in the centre for the lower limb, and my advice was to have an immediate operation with exposure of this region. Dr. Martin will describe the purulent meningitis found. The case brings up the important question whether the mere opening of the skull and exposure of the brain to the air may be beneficial in the treatment of meningitis in the way it sometimes is in a similar treatment of peritonitis. We would not, however, draw too sweeping conclusions from one case.

The swelling of the right eyelid might suggest thrombosis of the cavernous sinus, but such a lesion could not explain the meningitis beginning in the centre for the lower limb, and therefore near the superior longitudinal sinus. It seems probable that the infection was carried by a small vein from the nasal chambers or sinuses into the superior longitudinal sinus, and as comparatively few vessels empty into the anterior part of this sinus, the organisms might pass to the upper part of the brain before being arrested. The fibrous bands extending across the sinus would help to arrest the course of microörganisms, and the eddying of blood caused by the entrance of the cerebral veins into the superior longitudinal sinus in a direction opposite to the course of the blood in the sinus might aid in the deposit of the organisms at about the lower limb centre.

It is interesting to note that at first only a portion of the centre for the lower limb was affected in a purulent meningitis.

REMARKS BY DR. MARTIN.

This case suggested leptomeningitis secondary to what was almost certainly a frontal sinusitis and probably pansinusitis. Because of the swelling about the orbit the electrical trephine was first driven into the frontal sinus, which was found to be free of pus, though showing the evidence of a subacute inflammation. The posterior wall of the sinus was then drilled through, and a healthy non-adherent dura was exhibited. This wound was closed with drainage, fresh instruments were taken, and a large osteoplastic flap was turned down, exposing the Rolandic area almost to the central fissure. The dura seemed healthy. On incising it and turning it down, there was a free escape of turbid

fluid and a typical picture of leptomeningitis, most intense over the leg area, gradually becoming less marked when the face area was reached. A rubber wick drainage was inserted and the flap sutured in place.

Dr. Saxon, the resident physician, describes the condition following the operation.

The postoperative treatment was, of necessity, largely influenced by the irritability of the patient. Previous to the operation very little sleep was had, and afterward it was thought not advisable to disturb her for treatment. Moreover, treatments distasteful to her would cause great mental perturbation, which would last for hours. In consequence of this, such treatment as fractional doses of calomel, etc., had to be abandoned.

During the first five days following operation the treatment was directed mainly toward an effort to get free purgation, to induce sleep, and to correct the profound toxemia which existed. The first of these indications was by no means easy. As a result of the morphine which had to be given previous to the operation, there was a marked adynamia of the intestinal tract, and no bowel movement had occurred for two days. It was impossible to give castor oil or other bulky purgative. Because of this, calomel was given in three grain doses daily for three days, and was in each instance followed by liquor magnesii citratis, f℥v. Free purgation did not result until the fifth day following operation, and to accomplish this frequent enemata were given, and recourse was finally had to oleum tigli, ♏ij, and pulveris jalapi compositus, gr. xx. From the fifth to the twelfth day daily courses of calomel were given.

For the irritability and sleeplessness, morphine sulphate, gr. $\frac{1}{4}$ p. r. n., up to gr. $\frac{1}{2}$ in the twenty-four hours, together with sodium bromide and chloral, were used in large doses.

The treatment directed to the toxemia was continuous proctoclysis.

Because of a low tolerance to salt solution, no more than two and one-half liters in the twenty-four hours could be given. Great care was taken in this part of the treatment, because it had to be carried on in such a manner as not to disturb the patient; to this end an apparatus described in the March, 1908, number of *Annals of Surgery* was used. The proctoclysis was continued for a period of ten days.

It is needless to say that much of the treatment was purely symptomatic, and need not be mentioned here; but too much emphasis cannot be laid upon the efforts directed toward the establishment of free elimination, and this was accomplished by liberal purgation, continuous proctoclysis, and the frequent administration of water by mouth.

Throughout the mental crisis the diet was liquid. As soon as this sub-

sided, however, the patient's tastes were largely gratified, and she was given wholesome foods; pastries and sweets only were denied.

With the onset of convalescence the treatment was directed to the paralyzed muscles. The weaker groups, such as the anterior tibial and the extensors of the wrist and fingers, were given support to prevent contractures and tension, and they were exercised daily by the slowly interrupted, secondary current. Not more than ten contractions daily, of each group, were given.

When the case became ambulant, the treatment was mainly hygienic.

An examination made March 25, 1909, by the consulting physicians gave the following results:

The left foot can be moved a little, turned slightly inward, but the voluntary movement is slight unless the whole lower left limb is moved. There is much more power at the left knee and hip. Tactile and painful sensations are normal in left lower and upper limbs, and in the left side of the face. Ankle clonus and patellar clonus are pronounced on the left side. Patellar reflex much increased on the left side. The left hand cannot be moved at all except in associated movements. When she tries to move the left lower limb, or left shoulder, or to grasp with the right hand, the left hand is drawn upward by flexion at the elbow. She has slight power at the left shoulder, none at the elbow; the left biceps and triceps reflexes are exaggerated. Recognition of objects in the left hand is very imperfect, and sense of position is not entirely normal, though little affected. The left side of face in the lower part is still a little weak, but much power has returned. The left eyelids are not closed with quite the same power as are the right. The tongue is protruded straight. The general condition is excellent. Since this examination much improvement has occurred in the hemiplegia.

NOTE.—Since the above report was made complete recovery has ensued. The child has no trace of the hemiplegia, or any symptoms suggestive of her former serious condition, except that occasionally she has a left-side convulsion of slight intensity, and more frequent attacks of mild left-side paresthesia, usually confined to the left hand.

DISCUSSION.

Dr. Shields: I have seen the patient daily and can report a rather rapid continuous improvement. The muscles of the face have regained nearly their full power. She walks with only a slight limp, which is steadily improving, the previously fixed, extended, and inverted position of the foot having absolutely disappeared. The hand and arm are slowly regaining some power, as is shown by slight voluntary extension and flexion of fingers, and slight elevation of the arm. Patient's general condition is very good.

THE VALUE OF THE SALOMON TEST IN THE DIAGNOSIS OF CARCINOMA OF THE STOMACH.*

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(From the private laboratory of Dr. John H. Musser.)

The early diagnosis of carcinoma of the stomach is a matter of the greatest difficulty, and if one is to rely on the diminution or absence of free hydrochloric acid and the presence of lactic acid in the gastric contents, the morbid process is generally too far advanced to admit of more than a temporary benefit from operative interference. It was to overcome this distressing lack of early diagnostic measures that led Salomon,[1] in 1903, to publish the description of a method by means of which he hoped to facilitate the recognition of gastric carcinoma before it became too far advanced to be amenable to a radical operation.

The above-mentioned author believed that an ulcerating surface in the stomach must of necessity be associated with an outpouring of serum into that viscus, and he likens the process to the exudation of serum in slight face wounds after shaving. If the blood is stopped by using an alum preparation, for instance, the blood gradually disappears and serum takes its place, persisting for some time. A similar condition he supposes to be present in carcinoma, and he believes an examination of the washing from such a stomach would reveal the presence of albumin.

The danger of extraneous nitrogenous substances contaminating the gastric interior he guards against by the following technique.

* Read, April 7, 1909.

The patient receives in the morning only liquid diet, consisting of milk and gruel, and from two o'clock on bouillon, coffee, or tea. In the evening, at nine o'clock, the stomach is thoroughly washed out with large quantities of water until the wash water is perfectly clear, and after this nothing is given by the mouth. The next morning 400 c.c. of normal salt solution are poured into the stomach, withdrawn, poured back again, and again withdrawn, so that the entire gastric interior is mechanically flushed. In the wash water Salomon determines the nitrogen content by the Kjeldahl method, and the albumin by the Esbach tube.

He found in non-carcinomatous cases no reaction with the Esbach method, at the most a slight opalescence, and the total nitrogen lay between 0 and 16 mg. per 100 c.c. wash water. These benign cases included nervous dyspepsia, chronic gastritis, gastroptosis, acute gastritis, dilatation, hyperacidity, and chronic ulcer. He had no opportunity to study a case of fresh ulcer.

On the other hand, six cases of carcinoma showed in the wash water between 10 and 70 mg. nitrogen in 100 c.c., and between 0.0625 and 0.5 per cent. albumin, the albumin not bearing a definite ratio to the nitrogen. In his opinion, therefore, a carcinomatous growth should be suspected if the Esbach solution gives an immediate cloud or a determinable precipitate with the wash water, and if the nitrogen content exceeds 20 mg. in 100 c.c. fluid. He has not encountered any case of chronic gastritis accompanied by an albumin-rich excretion, nor has the same been met with in chronic ulcer, probably because the latter has already become cicatrized. Salomon claims that the presence of an ulcerative surface is improbable if the salt solution shows no cloud with the Esbach reagent.

Sigel[2] after a study of twenty cases was able to confirm Salomon's findings, with the exception that in ulcer and benign pyloric stenosis he found higher values than given by the latter author. In carcinoma the total nitrogen lay between 35 and 63 mg., and the Esbach method gave amounts varying between slight cloudiness of the reagent to 0.75 pro mille. As a result of Sigel's studies he is inclined to discredit the test as a differential diagnostic

measure between simple ulcer and carcinoma. This would seem to be of minor importance, as the two conditions are readily distinguishable. Sigel raises the limit of total nitrogen for benign cases to 25 mg., and says all values above this point to the probability of a malignant growth.

Berent and Gutmann[3] agree with Sigel, and believe the method useless if there is no ulcerating surface. They prefer to lay more emphasis on a positive result than on negative findings, for the above reason.

Reichenstein[4] discredits the test, inasmuch as in one case of gastric carcinoma he found very low values, and he suspects that positive findings are due to retained food rests which have not been completely removed at the time of the evening lavage.

Orlowski[5] holds a more favorable view, and regards the test as of service.

Schittenhelm and Lowes[6] never found as high a percentage of total nitrogen in chronic gastritis and benign ulcer as in carcinoma, and they regard the test as a valuable aid in the early diagnosis of malignant growths.

Zirkelbach[7] was able to confirm the results obtained by Salomon and other investigators, and he believes that with the exception of the rather rare forms of non-ulcerated carcinoma the test is a valuable aid in the diagnosis of malignant disease of the stomach. Zirkelbach raises the normal limit for total nitrogen to 30 mg., and to his mind all values above this point to carcinoma.

The chemical nature of the test seems to have been very thoroughly studied by Reicher,[8] and as a result of his observations he found that it depended on the presence of nucleoprotein and mucin. Serum albumin, contrary to the supposition of Salomon, was present either in only very small amounts or was absent altogether. According to Reicher, the test depends on the breaking down of cellular and nuclear substances rather than on a serum leakage.

Schupfer[9] says the test is of service if one remembers that there are occasional instances of a positive reaction in non-carcinomatous cases, while Romano[10] takes a more pessimistic attitude,

since he has obtained positive reactions in ulcerations of all kinds, also in cases accompanied with much mucus. Non-ulcerating carcinoma, on the other hand, gave a negative test.

Yagüe[11] tested the reaction in four cases of benign stenosis of the pylorus and in one case of hernia epigastrica with hyperchlorhydria, and in every instance found positive reactions. He regards the test as useless unless accompanied by other symptoms of carcinoma.

Witte,[12] after a study of sixteen benign and eleven gastric carcinomas, concludes that chronic gastritis, with great production of mucus, and simple ulcer are readily diagnosticated from carcinoma by this method. The results obtained in cases of gastrosuccorrhea were not definite. In the great percentage of cases of gastric carcinoma the diagnosis is materially strengthened by positive findings with Salomon's method. In cases with superficial infiltration and little ulceration the test may be useless. Witte regards a total nitrogen finding of over 25 to 30 mg. in 100 c.c. as pointing to carcinoma.

In all the twelve articles just quoted there has been no mention of control of the Salomon test in normal cases, and in certain diseases other than gastric conditions even Salomon publishes no report of such investigations. This seems to me to be a just ground for criticism, and while my studies of gastric disease were under way I endeavored to broaden the field of observation by examining the wash water from normal cases and from patients suffering from other than gastric disorders. The difficulty in obtaining normal cases for this work was removed through the courtesy of Dr. E. B. Hodge, who kindly permitted me to study the cases during Dr. Rodman's service at the Presbyterian Hospital.

Most of the remaining cases, gastric and non-gastric, were seen in the wards of Dr. J. H. Musser in the University and Presbyterian Hospitals, and in the writer's practice.

No.	Diagnosis.	Total N.	Esbach.	Phosphates.
1.	Normal case	0.0087	0	0.0050
2.	Normal case	0.0150	0	0.0075
3.	Normal case	0.0082	0	0
4.	Normal case	0.0490	cloudy	0.0060
5.	Normal case	0.0070	cloudy	0
6.	Normal case	0.0210	cloudy	0
7.	Normal case	0.0070	0	0.0020
8.	Normal case	0	0	0.0040
9.	Normal case	0	cloudy	0.0040
10.	Pernicious anemia	0.045	0.125	0.0060
11.	Pernicious anemia	0.0070	0	0.0040
12.	Pulmonary tuberculosis	0	cloudy	0.0030
13.	Pulmonary tuberculosis	0.021	0	0.0010
14.	Chronic nephritis	0.0210	cloudy	0.0020
15.	Chronic pancreatitis	0	0	0.0040
16.	Carcinoma pancreas	0.0190	cloudy	0.0020
17.	Persistent vomiting	0.0020	0	0.0020
18.	Hyperchlorhydria	0.0035	cloudy	0.0040
19.	Hyperchlorhydria	0.0245	0	0.0020
20.	Hyperchlorhydria	0.0070	0	0.0020
21.	Hyperchlorhydria	0	0	0.0040
22.	Hyperchlorhydria	0.0280	< 0.5	0.0060
23.	Hyperchlorhydria	0.0070	0	0
24.	Hyperchlorhydria	0.0170	0	0.0020
25.	Hyperchlorhydria	0	0	0.0020
26.	Hyperchlorhydria	0.0070	0	0
27.	Gastritis	0	0	0
28.	Gastritis	0.0100	cloudy	0
29.	Gastritis	0.0170	0	0.0020
30.	Gastritis	0.0210	0	0.0020
31.	Gastritis	0.0210	0.25	0.0020
32.	Gastric neurosis	0	0.25	0
33.	Gastric neurosis	0	cloudy	0
34.	Gastroptosis	0.0210	0.25	0.0010
35.	Gastroptosis	0.0240	0	0.0040
36.	Gastroptosis	0.0140	cloudy	0.0020
37.	Chronic ulcer	0	0	0
38.	Chronic ulcer	0	0	0.0040
39.	Chronic ulcer	0	cloudy	0.0060
40.	Chronic ulcer	0	cloudy	0.0020
41.	Chronic ulcer	0.036	cloudy	0.0020
42.	Chronic ulcer	0	cloudy	0.0020
43.	Acute ulcer	0.0385	0.25	0.0040
44.	Duodenal ulcer	0.0560	0.25	Not made
45.	Cirrhosis of liver	0.035	0	0.0020
46.	Cirrhosis of liver	0.021	0.0625	0

No.	Diagnosis.	Total N.	Esbach.	Phosphates.
47.	Carcinoma of rectum with metastases to liver and peritoneum; no gastric invasion	0.028	cloudy	0.0015
48.	Migraine	0.0140	cloudy	0
49.	Carcinoma	0.1540	Slight ppt.	0.0605
50.	Carcinomatosis, primary, in stomach	0.0070	cloudy	0.0750
51.	Carcinoma	0.026	0.5	0.1200
52.	Carcinoma	0.028	> 0.5	0.0060
53.	Carcinoma	0.0175	0.25	0.0140
54.	Carcinoma	0.052	> 0.25	0.0060
55.	Carcinoma	0.035	0.125	0.0040
56.	Carcinoma	0	0	0.0020

Normal and Non-gastric Cases. It will be seen from a study of the table that four of the normal cases gave a cloud with the wash water on the addition of the Esbach solution, and that two of these gave 49 and 21 mg. total nitrogen per 100 c.c., results which, according to Salomon, point to carcinoma. This condition was absent to a certainty, inasmuch as the cases were young individuals admitted to the surgical wards suffering from various injuries.

One case of pernicious anemia gave positive findings of 45 mg. nitrogen and 0.125 pro mille albumin. The diagnosis of carcinoma, despite this, was excluded, and the clinical course of the disease justified the original diagnosis of pernicious anemia.

One case of pulmonary tuberculosis had 21 mg. nitrogen. This case was admitted to Dr. Musser's ward in the Presbyterian Hospital with the diagnosis of gastric ulcer, but on examination this was excluded, and from the pulmonary signs, coupled with positive sputum findings, the diagnosis of tuberculosis seemed assured.

The only case of chronic interstitial nephritis had an absence of free hydrochloric acid in the gastric contents, and for the sake of completeness of the case record, Salomon's test was made, yielding 21 mg. nitrogen on examination.

Two cases of pancreatic disease, one case of persistent vomiting for which no organic lesion could be held as an etiological factor,

and one case of migraine, all yielded negative findings, but in a young man (No. 45), suffering with hepatic cirrhosis, a positive test was obtained, as was also the case in No. 46. No. 47 also gave a positive test, and not until operation was the diagnosis made with certainty.

Study of Gastric Cases other than Carcinoma. Nine cases of hyperchlorhydria were studied, and of these, two showed a nitrogen content above the limit for non-carcinomatous cases. Two of three cases of gastroptosis gave a positive Salomon test. In these two cases it may be argued that the high nitrogen figures were due to food rests which escaped the evening washing and first appeared after the morning lavage. There is no gainsaying this, but it hardly seems likely, as lavage was continued until the wash water came away clear.

Five cases of chronic gastritis were examined, two of which presented 21 mg. nitrogen. Of six cases of chronic ulcer studied, only one, No. 41, was positive, and this deserves a more than passing notice. The patient was a man, advanced in years, with pyloric stenosis and palpable thickening, myasthenia gastrica very marked, with accompanying retention, in whom the diagnosis of gastric carcinoma on the site of an old ulcer was made. At operation this was confirmed by the surgeon, and it was not until the specimen had been subjected to a microscopic examination that the diagnosis was made of a benign tumor of inflammatory nature.

Only one case of acute ulcer was examined, and, as was to be expected, with positive results.

Case 44, diagnosticated clinically as malignant, proved to be a duodenal ulcer. In this instance the high total nitrogen and the percentage of albumin spoke in favor of a carcinoma.

Gastric Carcinoma. Eight cases were examined, and in all of these the diagnosis was based on operative findings. Three of these gave a negative test, that is to say, in Case No. 50 the total nitrogen was very low and there was only a faint cloud with the Esbach reagent. Case No. 53 presented a slightly different picture, inasmuch as there was a determinable amount of albumin,

but a low nitrogen figure. Case No. 56 (a patient of Dr. Sailer) was examined with special interest. About a year ago the patient was operated on for carcinoma, the growth excised, and a posterior gastro-enterostomy performed. At the present time he complained of some tenderness in the right side, and a Salomon's test was made to determine the presence of a probable recurrence. The wash water contained not the slightest trace of nitrogen or albumin, and, as the patient complained of no gastric symptoms, it is fair to assume that the stomach was free from carcinomatous involvement.

In all my studies more importance has been placed on the Kjeldahl findings, as the Esbach method is so inexact that but little accuracy can be expected from its use. It is readily apparent, after studying the above table, that many conditions other than carcinoma are productive of results similar to those described by Salomon as occurring only in carcinoma. It may be that mucin has been the disturbing factor (Reicher) in our non-carcinomatous cases, and it may be that our positive normal cases were suffering with a low grade of gastric catarrh. If this is the explanation, the test loses the great diagnostic importance claimed for it, although Witte,* in his series of six chronic gastric cases, some of these with an abundance of mucus, found the highest total nitrogen to be 13.3 mg. In one the mucus was so excessive that the Ewald test meal had an alkaline reaction, yet there was only 9.1 mg. total nitrogen obtained. Be the explanation what it may, our results seem to invalidate many of Salomon's claims.

That acute bleeding gastric ulcer would necessarily be accompanied with high total nitrogen and much albumin was to be expected, but as the diagnosis between this condition and carcinoma rarely presents much difficulty, this finding (Case No. 43) in no way detracts from the value of the test.

An attempt has been made in this series to simplify the method and to remove from it three factors which would tend to prevent

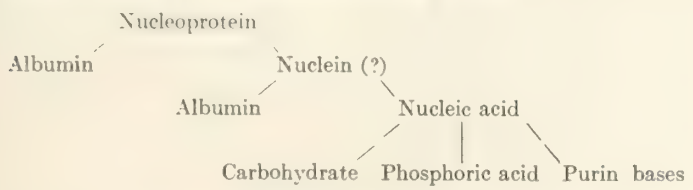
* Loc. cit.

its adoption by general practitioners. The first of these is the necessity for a special apparatus for determining the total nitrogen by the Kjeldahl method, and this apparatus is not usually found in a physician's laboratory.

Secondly, the estimation of the albumin by the Esbach tube takes twenty-four hours for its completion, and the results obtained are then so inaccurate that but little reliance can be placed on the method.[13]

Thirdly, the fact that any bleeding point in the stomach, being associated with an outpouring of serum, should be accompanied with a certain amount of total nitrogen and albumin varying with the extent of the lesion, would on theoretical grounds make the test valueless in such conditions. It was to overcome these objections that the estimation of the amount of phosphates in the wash water was undertaken in each case, as the method is simple and can readily be performed in any laboratory.

The hypothesis on which this test was based is as follows: The morbid anatomy of a carcinomatous growth is cellular. The essential part of any cell is the nucleus, which is composed for the most part of nucleoprotein. This nucleoprotein is made up of two chief components, an albuminous part and nucleic acid. The chemistry of the former, being of little importance in this discussion, may be disregarded. Phosphor is present in all nucleic acids, and phosphoric acid results as an end product of nucleic acid splitting together with carbohydrates and purin bases, as may be understood from the accompanying plan:



On purely hypothetical grounds, therefore, we believed that during the breaking down of a carcinomatous growth there would be a splitting up of the nucleic acid molecule, with the liberation of phosphoric acid.

Quantitative determinations of phosphoric acid were made in every case but one (No. 44), and in every instance, with the exception of the cases of carcinoma, the amount did not exceed 0.0075 gram in 100 c.c. wash water. In carcinoma, on the other hand, with the exception of cases No. 52, No. 54, and No. 55, there was a decided increase, 14, 60.5, 75, an even 120 mg. being obtained. In 48 non-carcinomatous cases, therefore, the percentage of phosphates was always below 10 mg., whereas in four of seven cases of certain carcinoma the percentage exceeded that figure. To explain the normal percentage in the three malignant cases, recourse must be had to theory by supposing that in those instances the splitting of nucleic acid into its end product, phosphoric acid, did not take place.

No claim is put forward that a phosphate yield of 10 mg. or more per 100 c.c. wash water is indicative of cancer of the stomach, but our results have been so suggestive that they are published in the hope that more work will be attempted along the lines of nuclein metabolism.

Conclusions. 1. Normal cases and cases other than gastric carcinoma are sometimes accompanied by more than 20 mg. nitrogen per 100 c.c. wash water.

2. Not all carcinomatous cases give a positive reaction, due probably to absence of ulceration.

3. The test is not pathognomonic, and can be regarded only as of doubtful assistance in conjunction with other features of the case.

4. The amount of phosphates in the stomach washings from a non-carcinomatous case is below 10 mg. per 100 c.c.

5. The percentage of phosphates in the washings of cases of carcinoma of the stomach usually exceeds 10 mg.

LITERATURE.

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CLINICAL NOTES ON ULCER OF THE STOMACH.[1]

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I HAVE in my hands a table of 6 cases of gastric ulcer which have been under my care recently and for which operations were done. My object tonight is to review briefly a few of the clinical features of these cases and say a few words regarding the diagnosis of gastric ulcer. The table is one of gratification on the one hand and somewhat of mortification on the other: gratification, because during the winter by means of operative procedure we have been enabled to relieve, perhaps cure, 4 cases of ulcer of the stomach; it has been a source of mortification in that 2 cases died, partly because of circumstances that ought to have been prevented. In the case of the male, aged thirty-seven years, I must confess that death took place because of my own deficiencies. The man could not give a very good statement as to his symptoms, and it was rather difficult to determine the clinical course, or to appreciate, rather, the symptoms that the man presented. Then, too, there was some slight defect, which, unfortunately, will occur sometimes in hospital technique, which prevented an operation being done upon the man as early as it should have been, and in consequence death took place from hemorrhage. Perhaps, had I been a little more astute, and the operation been conducted earlier, his life might have been saved.

In the second instance, in the patient, aged fifty-six years, also a male, death took place because he would not submit to operation until he was practically a dying man. He had been

[1] Read April 7, 1909.

under observation for two years. Pyloric obstruction the result of ulcer was diagnosticated. He was constantly importuned to submit to operation, but without assent on his part.

The remaining cases got well, although I am bound to say that in one instance operated on by Dr. Frazier the time elapsed is only six weeks, and yet I must say that in this case the cure has seemed really more positive than that of any of the others. Yet the short time might afford criticism that the case should not be reported cured as yet.

The clinical course of the disease as exhibited by this small group of cases, and also a larger number which I have had the opportunity of studying, satisfies me, as I think we all agree now that the old-time definition or description of gastric ulcer scarcely obtains, and that, while pain and vomiting and hemorrhage are undoubted symptoms of this affection, yet in their association with functional acts of the stomach they differ entirely from the statements that formerly have been made. Indeed, I feel now that in making a statement as to the symptom complex of gastric ulcer, remembering, of course, the age, sex, and causal factors, we should state that the phenomena are those of hyperchlorhydria or of hyperacidity in the larger proportion, practically in all cases, plus the phenomenon of pyloric obstruction, temporary or constant.

In this group alone vomiting was not the frequent symptom that we are led to believe is present in this affection. Pain had not the characteristics that were originally taught us as occurring immediately after food, relieved by vomiting, and attended by local tenderness increased by pressure. Pain in all instances occurred at longer periods after the taking of food. It occurred at the height of gastric digestion, or two or three hours after eating, and was always associated with the phenomenon of pyloric spasm the result of hyperchlorhydria.

The pain was not in the epigastrium except in one case. It was either over the pylorus, or, as in two instances, far to the left of the abdomen, and, in the case of a poor fellow who died, was confined almost constantly to the region of the spleen or

even above. It was the result of distention secondary to pyloric spasm. The pain, therefore, of gastric ulcer is usually not really the pain due to the irritating action of the food on the ulcer, but is due to the irritating action of an excess of hydrochloric acid, or due to pyloric spasm, or due to the distention that occurs secondarily to pyloric spasm. For each of these causes the pain has a special characteristic. In the first instance it is a gnawing, boring, dull pain or an agonizing "gone-like" sensation. In the second it is wave-like or gripping, and corresponds to rhythmical contractions. Peristaltic waves may be seen. In the third there is fulness or distention, with crowding of the diaphragm and heart.

Hemorrhage occurred in 2 of the cases, and hemorrhage is perhaps the one symptom concerning which our ideas, based upon the text-books of ten or twenty years ago, need not be changed. It is certainly a most important sign of ulcer, whether present grossly in the vomitus or found in the stools, or whether determined by methods which disclose occult blood.

In 2 of our cases only was occult blood found in the stools, and in 2 only was there hematemesis.

The other determining feature that one must consider in deciding the presence of gastric ulcer is the remissions in the course of the disease. This was characteristic in nearly all of the cases. There would be quite deceptive periods of relief. Indeed, I might say in all the cases there were periods of relief when the patient would congratulate himself that he was well. Such remissions are so suggestive of the actual nature of the lesion that they become an important point in the diagnosis. Thus, for instance, in the third case, the woman, aged sixty years, who had all the grave symptoms of ulcer of the stomach in the early spring, was wonderfully relieved symptomatically during the summer and gained some ten pounds in weight. In the fall, after exposure and some depression during the period of the celebrations in October, she went down again with recurrence of the symptoms. I might say, parenthetically, that I do not believe we take into consideration in gastric cases the gravity of the effects of exposure; that there will be recurrence of forms of

gastritis and definite relapses, not after the dietetic errors, but after chill, and perhaps a little period of fever; or, after the phenomenon of an ordinary "cold" there will be a recurrence of gastric symptoms. In this instance the second period of symptoms were so very grave, the fall in the blood count, the loss of weight, and the rapid prostration were such that we were very much afraid that there was malignant disease. But we supported our belief by the fact of remissions that ulcer was present and urged operative procedures. This was carried out by Dr. Martin and two ulcers found, one adherent to the pancreas and the other in the pyloric end of the stomach. The probabilities are that the first ulcer might have been the cause of symptoms and that the second ulceration had occurred early in the fall.

I want to say a few words regarding the symptoms of hyperacidity which are significant in ulcer of the stomach. One is the persistent vertigo that often attends a hyperchlorhydria, and which continues until the hyperchlorhydria is relieved. The others are the symptoms of hyperacidity whether from a total excess or an excess of HCl the extreme distress in the esophagus, and the distress in the stomach, the result of the direct local action of the hyperacid gastric contents with constant regurgitation of the acid fluid. Curiously these two symptoms were most marked in a mother and her daughter. In the mother they had occurred through a period of fifteen years, and the acidity was so extreme that she had taken pounds of soda each year. To such an extent was this true that her husband facetiously said that he would be able to save on the soda account sufficient to pay the surgeon. The daughter, for similar reasons, from her eleventh to her twenty-first year was also a soda fiend, and had to take enormous amounts in order to obtain pronounced relief. It was on the persistence of and the absolute inability to relieve these symptoms by all medicinal means known to us that supported me in advising strongly operative procedures. In both cases there was pain, but not sufficiently classical to say that it was the pain of ulcer of the stomach alone. In one case there was a history of hemorrhage from the stomach, and in the other there was a

history irregularly of occult blood which we thought we could trace to the lesion of the stomach. Both were kept in bed at rest for long periods of time without benefit. Since operation done in the early winter there has been relief to these strikingly persistent and extraordinary symptoms. This is all I shall say with reference to the clinical course of the disease and the phenomena upon which we can base a diagnosis.

I think it would be of interest to tell you that the amount of total acidity and of free HCl was in every instance, with the exception of one, very high. In the poor fellow who had an ulcer of the pyloric end of the stomach the total acidity was as high as 120, and repeated analyses made gave the free HCl as 80.

I have reason to believe, from the fairly large experience I have had, that the diagnosis of gastric ulcer is very difficult to make, certainly not one that can be made off-hand. We cannot make a snap diagnosis of the affection. But the responsibility is a great one, in obscure cases, to advise a person to have an exploratory operation. Indeed, the more I see of surgery the more I feel that we must go very slowly in our advice to patients with regard to abdominal section. I feel that this is particularly true unless I have the opportunity of also advising the surgeon who is to perform the operation. Under certain circumstances the operation is extremely grave. I am bound to say that I have advised exploratory operations that were not done for which I have had considerable regret. I am bound to say that I have not had any exploratory operations done that I have ever regretted, except in instances where I could not select the surgeon. The surgeon, or the embryonic surgeon, devoid of experience, who, after having had my advice as to the wisdom of operation, performed the operation, and found conditions which he could not meet without disastrous results. I feel, therefore, that we as clinicians should consider carefully while the patient is under observation a fair period of time before coming to a conclusion as to surgical interference in ulcer of the stomach, and then we must have the right to select the surgeon. In some instances a decision can be arrived at immediately, in others observation must be prolonged.[1]

[1] See Trans. Congress of Physicians and Surgeons.

I still feel that the disease is not a common one.

From the statistics which I have arranged, notwithstanding those of the English surgeons and perhaps of some other surgeons in this country, I still feel that it is not a very common disease in this community.

Furthermore, I feel that there are circumstances quite abundant when medical measures can bring about relief and perhaps cure in a certain proportion of cases, namely, in those that are acute and hence have had symptoms for a very short time.

The clinical course of the disease, as I have attempted to portray, plus the one fact of remission, supports one in the diagnosis of this affection, particularly—and this is what I wish to emphasize—if we recognize that the symptoms of ulcer are those of hyperchlorhydria plus those of temporary or permanent pyloric obstruction.

Finally, I wish to repeat, the picture of gastric ulcer, especially of chronic ulcer, must be that of a non-febrile gastric disorder, attended by remissions, with symptoms of hyperchlorhydria or hyperacidity and of temporary or permanent pyloric obstruction, and of fairly constant findings of blood and of HCl excess.

DISCUSSION.

Dr. John B. Deaver: I have been impressed with Dr. Musser's statements as arguments in favor of early operation. Dr. Musser relates one case under observation for over two years before being operated. I am wondering how long this patient might have lived had the operation been done in the early part of his illness. I feel in regard to abdominal disease that he who deliberates is lost—if he deliberates too long. Certainly he will lose the majority of his patients.

In the question of diagnosis I agree with Dr. Musser entirely. I do not think there is any more difficult diagnosis to make at times than that of gastric ulcer. Take the question of gastric ulcer, duodenal, and certain cases of gall-bladder disease, and it is impossible for any living man to always make a diagnosis with certainty. Under these conditions the patient is a subject of dyspepsia, of an indigestion, and crystallized gas is formed in the shape of gallstones. In such a patient the physician is censurable, if at the end of two or three months expected relief is not obtained, if he does not recommend

an abdominal operation. I say that advisedly, as I have the support of the best surgeons in this country and on the Continent. We must not close our eyes and ears to the statements of men who are opening bellies by the hundreds.

I am rather surprised that Dr. Musser hesitates to advise abdominal exploratory operation. I never have seen any bad effects of simple abdominal exploration. I should rather have my abdomen opened than to be dosed with subnitrate of bismuth and have an *x*-rayist observe it for three hours.

We surgeons must admit that all of our patients do not get well. I see patients every now and then who are believed to be well, ready to go out of the hospital, fall over dead. That occurs to the people walking on the streets who have not had any surgery done. I see an occasional case of pulmonary embolism. I do not see peritonitis, sepsis, and death following these operations. Therefore, to my mind, it is a question, Shall we take the risk of one of these remote possibilities which do occur in a small percentage, or the greater risk of the results of this pathological condition? In my experience as a surgeon it is not the disease which troubles me, but the results of the disease. We all admit that if we can take out the appendix and the disease is confined to the appendix there would be no deaths. It is the resulting peritonitis and its consequences that trouble us. So with gastric ulcer. Operation for gastric ulcer is a simple matter in the majority of cases. In cases of acute gastric ulcer I think surgeons generally would not advise operation. Those cases belong to the medical man and should not be touched. I have on one or two occasions operated on such cases with unfortunate results. Dr. Tyson will recall a case seen in consultation on Green Street in which the lady had had a severe hemorrhage. Operation was done and the patient perished.

Surgeons, I believe, will come more and more to the operation of excision. Dr. Musser suggested that very wisely. While we are not able to say from touch or sight whether or not indurated ulcers at the pylorus are malignant, if there are perigastric adhesions a pylorectomy should be done. In my hands this condition is attended with better ultimate results than posterior gastro-enterostomy.

I am well pleased with the results of gastro-enterostomy as reported by the Mayos, Moynihan, Robson, and myself. After five years' work with this operation in the German Hospital we are able to report 60 per cent. of cures. I think this is a sufficient time upon which to estimate a cure.

While I do not place much reliance upon the presence of occult blood, yet I admit it plays a role.

Dr. S. Solis Cohen: Confirmatory of the point brought out by Dr. Deaver of the difficulty of diagnosis between affections of the gall-bladder and ulcer of the stomach, I have had recently some very striking experiences. Three cases may be cited: The first was diagnosticated as gallstones or

empyema of the gall-bladder, a view concurred in by Dr. Chalmers Da Costa, who operated and found, indeed, the gall-bladder adherent to the stomach wall, but at the site of an ulcer ready to perforate; in the second case, reversing Dr. Deaver's opinion of the comparative readiness of physicians and surgeons to operate, I had asked a surgeon to undertake section for exploratory diagnosis. He declined, saying that it would be "a reproach to surgery" to open that abdomen. Another surgeon consented to make the exploration. I was in doubt as to the exact condition, but inclined to think it one of indurated gastric ulcer, or perhaps carcinoma, because of a vague mass which I had felt through the thick abdominal wall in the region of the pylorus. Neither of the surgeons was able to confirm this finding, but upon the history of persistent pain, recurrent abdominal distention, and loss of weight, exploration seemed justified, and we found upon section that the mass was a large gall-bladder containing a quantity of thick, black bile and several stones. In this case there was no jaundice, unless a very slight yellowish tint of the conjunctiva be so interpreted; there was obstinate constipation, but the stools were of normal color and the urine free from bile or urobilin. Cammidge's reaction was found and occult blood detected both in the stomach contents and the feces; acidity was normal. The third case was sent down from the country with a diagnosis of appendicitis. The patient arrived at the hospital in a desperate condition, and prolonged examination was out of the question. The symptoms of general peritonitis with previous pain referred to the hypogastrium, the high leukocyte count, the low temperature, with such history as we could obtain, suggested perforating duodenal ulcer. Appendicitis was considered and excluded. Dr. Gibbon operated and found a gangrenous gall-bladder with the largest number of very small stones that either he or I have ever seen.

I fully agree with Dr. Deaver in the necessity for early operation and especially for early exploratory incision—exploratory diagnosis—in obscure affections of the upper abdomen. I confess that, when obscure, it is for me, at least, the most difficult region in the body. Diagnosis of diseases of the chest is child's play in comparison.

I may allude to dangers which Dr. Deaver has not mentioned among the consequences of allowing gastric ulcer to go without operation. In one case operated upon for me at the Jefferson Hospital by Dr. Da Costa the patient had been under the care of a good physician for some time, suffering intense pain. She had been given a good deal of morphine to relieve the pain. Dr. Da Costa found upon section what we had both judged to be present—an indurated gastric ulcer. The patient made a good recovery from the operation, but the difficulty in that case is going to be the morphine habit. That is a danger not to be ignored when we decide to permit these painful conditions to continue without making some attempt at radical relief.

Apparent recovery from gastric ulcer may not mean freedom from ill consequences. I have before cited, in discussion before this college, the case of a girl, one of my early patients, who recovered from gastric ulcer attended with hemorrhage, under medicinal measures, and who eighteen years later had a recurrence of symptoms and refused operation which I then proposed, on the ground that in the previous attack, when she was much worse, I had not counselled surgery and she got well; while this time she was not so sick, and therefore would not be operated on. She has, indeed, recovered from the acute symptoms, but now has constant distress, which I attribute to adhesions and to the poor functioning of the stomach because of distention. I rather regret that at the time when operation might have been attempted it was not done, although it is true that very few surgeons were then willing to operate.

I am not sure that the majority of cases of gastric ulcer as they have come under my own observation, have been attended with notable hyperchlorhydria, or that the symptoms can always be referred to hyperchlorhydria. That it has occurred in the majority of reported cases is unquestionable, but I have seen a few cases, as Dr. Musser, of course, has also, in which there was subacidity rather than hyperacidity. Yet in some of these cases the diagnosis was clearer than I have found it in a number of hyperacid stomachs. Dr. Musser is beyond doubt in his position that persistent hyperchlorhydria should raise the question of gastric ulcer and is to be reckoned among confirmatory symptoms; yet we must not therefore be tempted to conclude that the absence of hyperacidity puts aside that diagnosis. Nor do I understand Dr. Musser so to conclude, though I have heard the argument made by others. The question of the time of pain is quite important. I have been paying special attention to that since the classic descriptions have been challenged, by the modern surgeons especially. In the few cases I have seen I think it occurs at almost any time. It may come on in some cases immediately after eating, and in others without any relation whatever to the taking of food; and the location of pain, or tenderness, while very frequently in the classic epigastric spot, may be almost anywhere above the umbilicus.

In conclusion I desire simply to say that I believe both physicians and surgeons can profitably confess the inadequacy of present diagnostic means to determine accurately the exact nature of morbid conditions in the upper abdomen, and that exploratory incision is justified when, after sufficient and not too prolonged study, diagnosis is otherwise impossible; provided, of course, that there is good ground to suspect a condition susceptible of surgical relief. Twice I have had section made for gallstone which was not found; in each instance the patient made a good recovery, and lost her symptoms. I do not regret either incision, but I should regret failure to give timely counsel for incision and operation in any condition demanding surgical relief.

Dr. William J. Taylor: I should like to ask Dr. Musser whether in his use of the word "operation" he means that a posterior gastro-enterostomy

was done, or whether there was any other operation done upon the stomachs of these patients.

Dr. Musser, in closing: I thought I had aligned myself pretty closely with the surgeons in reporting 6 cases operated on in a period of three or four months, and so cannot be accused of withholding operative procedures or exploratory procedures. The case Dr. Deaver refers to incorrectly I stated absolutely refused operation for two years. However, I still feel that the tendency is too strong to operate before we know enough about the case. There should be careful observation by the internist, and we should be able to say to the family that the operation is done for such and such conditions. It is quite proper to take sufficient time to study the case and make a correct diagnosis, which, with time, I think can be done in nearly all cases.

In only one of the cases do I feel that I was culpable in postponing operation, postponed because of my stupidity. I did not appreciate the clinical picture and did not understand the man's language, and then, when we decided upon operation, there were some technical difficulties in the hospital management which made it so late that the man had very grave hemorrhages and death took place in spite of operation.

Of course, the presence of occult blood in the stools does not mean anything at all unless one very carefully weighs all the circumstances under which blood may be present which would respond to the test. The man must be meat-free. When under all such circumstances we find occult blood, we can rely upon it with a considerable degree of safety.

Posterior gastro-enterostomy was done in 3 cases and resection of the ulcer in 3.

A CASE OF ESSENTIAL PENTOSURIA.[1]

By SOLOMON SOLIS COHEN, M.D.,
PHILADELPHIA.

The old dictum that life is the chemistry of carbon receives additional illustration in the anomalous condition known as pentosuria—the presence in the urine of the pentatomic form of sugar. It constitutes as yet little more than a clinical curiosity, but suggests many important questions, whose answers, when found, will doubtless be illuminating as to certain dark corners of the field of metabolism.

Pentose is a species name rather than an individual designation. It is applied to a group of some eleven monosaccharids, having the general formula $C_5H_{10}O_5$, and thus differing, by one carbon atom and the elements of a molecule of water, from dextrose, levulose, galactose, etc., which, containing six carbon atoms in the molecule, are termed hexoses. But this apparently slight chemical difference is of considerable physiological and pathological importance. The sugar which appears in the urine in diabetes mellitus is dextrose; and, as we all know, its presence usually indicates a profound and often dangerous disorder of metabolism, associated with distressing symptoms and having a somewhat uncertain dependence upon more or less definite structural lesions. While hexosuria is thus potentially and often actually grave, pentosuria, on the other hand, is essentially mild. It is unaccompanied with the polyuria, polydipsia, and bulimia of saccharine diabetes; it is not characterized by emaciation or by obesity; and so far as yet appears is unattended with special

[1] Read May 5, 1909.

liability to pyogenic and other infections or with the risk of acid intoxication. Of its possible association with definite tissue changes or circulatory disturbances nothing is known.

Urinary dextrose is optically active; as the name implies, it rotates the polarized ray to the right. Being a reducing aldose, it is commonly recognized by its power to precipitate metals or their oxides from solutions of metallic salts, especially those of copper and bismuth when heated with an alkali. It is fermentable with yeast. These properties are manifested by the hexoses in general, as well as by the disaccharids —for example, sucrose and maltose— which contain twelve carbon atoms, and may, by the hydrolysing action of dilute mineral acids, be made to take up the elements of an additional molecule of water and separate into two hexose molecule groups. The pentoses are likewise reducing aldoses. They behave much like dextrose with the bismuth test of Boettger, but the reduction of metallic bismuth is usually incomplete and the precipitate is brown or gray, rather than an absolute black. With Fehling's solution, they give a peculiar reaction, producing somewhat suddenly, after some minutes' boiling, a heavy greenish or yellowish or orange-colored precipitate in place of the red or salmon-colored oxide with whose gradual development we are familiar. While decomposable by the action of certain bacteria, and especially the intestinal flora, they do not, however, ferment with yeast, and their bacterial decomposition is not attended with the evolution of gas. Consequently, in the examination of a specimen of urine which reduces bismuth imperfectly and gives an anomalous or incomplete copper reduction, the failure to ferment, more especially if polariscopic examination shows the reducing substance to be optically inactive, should direct attention to the possibility of the presence of a pentose. Diabetes mellitus is in such instances excluded; but other chemical tests must be made before the identity of the reducing, non-fermentable substance can satisfactorily be established. The most difficult discrimination is that between glycuronic acid and pentose. In the case which I report herewith I availed myself of the chemical skill and knowledge of Professor Charles H. LaWall to make this dis-

crimination, and he has kindly consented to report the results of his tests and to explain their significance. While optical inactivity is almost conclusive, both against dextrorotatory glucose and levorotatory glycuronates, it must not be forgotten that many of the pentoses are optically active; and at least one of these has been known to appear in the urine. The crucial test is the recognition of the melting point of the crystals of pentosazone produced by the action of phenylhydrazin. Spectroscopic examination, moreover, shows different positions of the absorption bands of the substances produced by the action of various reagents with glycuronic acid, dextrose, and the pentoses.

The pentose group of saccharids—or, more correctly, certain anhydrides, called pentosans, which bear the same relation to the pentoses that starch, for example, bears to dextrose—are widely distributed, if not universally present, in the vegetable kingdom, being found in fruits, leaves, stems, and roots. The legumens, and, among fruits, the pear, are especially rich in pentosans. The nucleinic acid of the embryos of wheat was found by Osborne and Harris to contain three molecules of pentose to each 4 atoms of phosphorus. Pentose has been demonstrated by Kossel and Neumann in the nucleinic acid of yeast, and Bendix, as well as Aronson, has found it in bacteria, including pathogenic forms, as tubercle and diphtheria bacilli. The most common forms of vegetable pentose are those termed l-arabinose and l-xylose. In the animal body, pentose was first discovered by Hammersten as a constituent of the nucleoproteid of the pancreas. The substance thus discovered has been identified as l-xylose. Since then various observers have demonstrated its presence in the liver, the thymus, the thyroid, the spleen, the kidney, the muscles, the brain, and the mammary gland, and it is, in general, supposed to be a persistent constituent of the nucleus; so that it is most abundant in those tissues that are rich in nuclei. Nevertheless, the whole amount contained in an ordinary adult human body has been calculated as not more than about 10 grams.

Pure pentose, when given to man or the carnivora by the mouth or injected into the blood, may be in small part assimilated;

but it is usually, for the most part, rapidly excreted in unaltered form in the urine. Nevertheless, large quantities of pancreas or of vegetable foods containing pentosans may be ingested without the production of an alimentary pentosuria; probably on account of the slowness with which the saccharid is set free from its proteid combinations. The discordant results obtained by various observers in regard to the quantities of pentose recoverable from the feces and urine when pure xylose or pure arabinose has been administered by the mouth, are to be attributed in some measure to its decomposition, with the formation of lactic acid and alcohol, by the intestinal bacteria; and this process probably tends also to prevent alimentary pentosuria under ordinary conditions. While the pentosans and pentoses seem to play an important part in the nutrition of herbivora, no animal or vegetable enzyme that will hydrolyze pentosans has been demonstrated with certainty; and the physiological questions concerning their assimilation and utilization are as yet quite unsettled.

When alimentary pentosuria is induced by the feeding of pure pentose, the form that appears in the urine is the dextrorotatory l-arabinose,[1] whereas that which appears in essential pentosuria is the optically inactive r-arabinose. The apparent exception reported by Luzzato is attributed by some critics to a transient alimentary pentosuria accompanying the essential form. Urinary pentose is supposed to be excreted in combination with urea, as an arabinoseureid. To this fact is to be attributed the slow reduction giving rise to the peculiar reaction with Fehling's solution, for the sugar must first be set free from its proteid combination by the action of the heat and alkali, and this decomposition occurs only after some minutes' boiling. In fact, in the first examination of the specimen from my own case I was unable to get any response to Fehling's test until I had added a decided excess of alkali.

[1] The letters d- and l-, as prefixed to the names of the various pentoses, are as likely to be confusing to other physicians who do not happen to be expert chemists as they were to the writer of this article until he learned the facts. One would naturally suppose that d-arabinose is dextrorotatory and that l-arabinose is levorotatory, but the exact contrary is the case. The letters do not indicate the optical activity of arabinose, xylose, etc., but that of the hexose molecules with which the pentoses are respectively chemically homologous.

Pentosuria was first clinically recognized in 1892 by Salkowski and Jastrowitz. The patient happened to be a person addicted to morphine, and his drug habit was supposed to have some causal connection with the condition. This idea, however, has been disproved. In 1895 Blumenthal reported two additional cases from Salkowski's laboratory. Since then a number of cases have been reported, most of them, however, from the First Medical Clinic in Berlin and Salkowski's laboratory. Neuberg identified the urinary pentose as r- or racemic arabinose, which is optically inactive, but may be decomposed into dextrorotatory and levorotatory constituents. Luzzato, however, found the pentosazone obtained from the urine of his patient to be slightly dextrorotatory, corresponding in this respect with the pentosazone of the l-arabinose of the vegetable kingdom. In my case a dextrorotation of scarcely 1° was found on one occasion only. The significance of this will be discussed later.

Three varieties of pentosuria have been recognized:[1] (1) *Alimentary pentosuria*, in which the phenomenon follows the ingestion of food rich in pentose-producing substances. (2) *Complicating pentosuria*, in which the urine contains both pentose and hexose—the cases being actually diabetes mellitus, and the small quantities of pentose transiently present having no known clinical significance. Similar to these cases are the instances of experimental pentosuria found to accompany the diabetes mellitus of dogs deprived of the pancreas or poisoned with phloridzin. (3) *Essential pentosuria*, in which the excretion of pentose is persistent, independent of diet, and not associated with diabetes mellitus. It cannot be said, nevertheless, that in essential pentosuria there is no association with hexosuria. The relation, however, is the reverse of that obtaining in complicating pentosuria. It is now the dextrose that

[1] The substance obtained by Cammidge from the urine of patients having pancreatic disease is also supposed to be a pentose. In a recent case of my own showing a slight Cammidge reaction, glucose was excreted for a few days; and then a reducing, nonfermentable substance not yet identified. A similar series of phenomena occurred in the case of an obese woman of diabetic and carcinomatous heredity, and marked vasomotor ataxia of the menstrual variety, suggesting a possible origin in pancreatic circulatory disturbance. This case is reported in my paper on "Visceral Angioneuroses," read before the Association of American Physicians, 1909.

appears transiently and in minute quantities, and even this has been recorded in but a few cases, of which my own appears to be one.

According to T. C. Janeway, who, in 1906, reported two cases of essential pentosuria in brothers, there had been previous to his report but seventeen indubitable cases placed upon record, of which one came from Italy and two from Norway, but none had been found in British, French, or American literature. So far as I know the present is the fourth case observed, and the third case to be placed upon record in the United States. Added to the seventeen cases collected by Janeway, with the two reported, and two others (unpublished) alluded to by this author, it would make twenty-two in all. I have not, however, searched the literature since Janeway's report, and there may be a few more. At all events, the total number of cases recorded in the seventeen years elapsing since the first clinical recognition of the condition has not reached forty. For this reason, isolated cases are still worthy of report.

My patient is a married man, a native of one of the middle Western States, aged fifty years. He has never had any venereal infection. He uses alcohol rarely and tobacco moderately. He is a leading member of the bar of his State, and is frequently required to appear in the Supreme Courts of other States and of the United States. It may, therefore, fairly be said that he has been engaged for many years in arduous, sometimes exhausting, mental labor; and, if we consider the strain of travel and of pleading, in physical labor as well. However, he has the vacation habit well established, and except for an occasional European trip, usually spends his summers in the woods or mountains, or on the Maine Coast, tramping, boating, fishing, hunting, or loafing, as the environment and his mood may suggest. When at home he rides and golfs as opportunity offers. He does not, therefore, strictly speaking, lead a sedentary life. He has recently—that is to say, for some four or five years past—been actively engaged in a movement for reform in the government of his city; and has had in connection therewith the burden of preparing important legal cases

against a number of eminently respectable citizens. It is to be supposed, therefore, that he has been under a severe mental strain.

While he exhibits some of the signs of vasomotor ataxia, he is not what is commonly termed neuropathic; and there is not in his family any history of neuropathic, arthritic, malignant, tuberculous, or diabetic affection. Cutaneous affections have been present.

He first came under my care about fifteen years ago with symptoms of subacid gastro-enteric indigestion. Recovery took place under lavage, gastric faradization, and regulation of diet and exercise. The urine showed an excess of indican, as well as of uric acid, urates, and oxalates, but contained no albumin, sugar, or casts. An attack of furunculosis some years later made me study the urine carefully and persistently for glucose, but none was found. The patient has had from time to time brief periods of indigestion, sometimes a transitory constipation; but there has been no significant ailment of any kind. He has had periods of genuine and well-earned fatigue, but no neurasthenia. He has seen me at least once in every year, often more frequently; and I have probably examined his urine three or four times in each year, finding neither albumin nor sugar. He has also consulted, when necessary, a leading physician of his home city, one of my own pupils, whom I have associated with me in the case. It is unlikely, therefore, that any pathological occurrence would go long unnoticed.

In March, 1908, a life insurance examiner postponed his application, and he learned indirectly that it was on account of the urinalysis—albumin was said to be present. There was no suspicion, apparently, of sugar. The local physician examined the urine and found no albumin, but an anomalous reduction with Fehling's solution. He suggested that diabetes might be impending, but in the total absence of symptoms hesitated to make the diagnosis. A specimen of urine, taken from a twenty-four-hour collection amounting to 1500 c.c., was sent to Philadelphia. I found it to be clear, amber in color, 1023 specific gravity, acid in reaction, giving a brownish precipitate with bismuth subnitrate and potassium hydroxide, a greenish yellow precipitate with

Fehling's solution, and no gas upon attempted fermentation with yeast in Einhorn's saccharometer. There was no albumin; casts were not detected. A few leukocytes formed the only microscopic finding. Suspecting pentose, I enlisted Professor LaWall's coöperation, and, studying the specimen with him, we found it to give all the pentose reactions, but in exception to be slightly dextrorotatory. A few days later the patient himself arrived. Careful physical examination showed nothing abnormal except a very slight enlargement of hepatic dulness, which had been present for some four or five years, and a very slightly increased arterial tension, not high enough, however, to indicate pathological change in the arteries. The blood was normal to microscopic and color study. The eye ground had been examined by a local oculist, and was reported to be normal. The patient had gained some twenty pounds in weight during the last five years, but was not pathologically obese.

I have, in conjunction with Mr. LaWall and the local physician, kept the patient and the urine under observation, more or less closely, ever since; that is to say, for more than a year. Twice during that time he has complained of lassitude and indisposition to work—symptoms quickly disappearing after a few days at Atlantic City, or the brief administration of lecithin or glycerophosphates. Milk diet, flesh diet, diet with and without the ordinary carbohydrates, and diet with and without substances rich in pentosans, have been instituted, for brief periods only, it is true, as the patient's activity does not lend itself to overmuch regulation or restriction. There has been practically no change in the urinary findings, except that although Mr. LaWall has not again found any dextrorotation, the local physician in February of this year did find, on one occasion, a few bubbles of gas, and on another, a reading of 0.25 per cent. by gaseous column, in Einhorn's saccharometer. I did not have either of the specimens, and cannot confirm the observation; but I do not doubt its accuracy. This would seem to indicate some transient complicating excretion of a fermentable sugar (and, since the paper was read, a small quantity of hexose has again been found, as set forth in footnote).

There is no instance on record of the transformation of pentosaria into diabetes, yet while knowledge remains so limited, care is necessary. I therefore thought it well to test dextrose assimilation more particularly. For this purpose I gave the patient, by the mouth, on each of two successive days, 100 grams of the glucose of pharmacy in two portions; and with Mr. LaWall examined the total urine of the forty-eight hours. In this there was no trace of any excreted hexose, but pentose was found as before. No excess of indican has been found in the pentose-containing urine although this was occasionally present before the pentosuria was discovered. The excretion of urea continues around 3 per cent. The chlorides in the last specimen were 0.94 per cent., or about 15.46 grams. The phosphates, estimated as P_2O_5, were 0.3 per cent., or 4.8 grams, a slight increase over the normal average. The total sulphates, being 0.31 per cent., or 5 grams, of which 0.3 per cent. represents preformed salts, show also a slight increase; while the rather low ratio of conjugate to fixed sulphates, 1 to 30, especially when taken in connection with the low indican content, would show a relative absence of intestinal decompositions. Bacterial study of the feces is therefore desirable, for a question is raised as to the possibility of absence or partial destruction of intestinal bacteria as a factor in the production of the pentosuria. Whether or not this study can be carried out, I do not know, but it calls for attention. The salol test does not indicate any failure of the secretion that splits this drug.

I have not specially experimented with the feeding of sucrose, levulose, lactose, etc., or with any pure pentose; but hope to have the opportunity to make these and other observations from time to time, as the patient finds opportunity to visit Philadelphia, or we succeed in enlisting expert chemical assistance in his own city.[1]

[1] Our patient, however, informs me that I have "overestimated his zeal for scientific research." He consented, nevertheless, to visit Berlin, while in Europe this summer, and to see Dr. Jastrowitz, who writes as follows:

"Both Professor Salskowski and I can, from careful studies, entirely independent of one another, confirm your diagnosis of pentosuria. The first time that the patient brought his urine to me, I found in addition to pentose $\frac{1}{6}$ per cent. of hexose, but although I had the urine of various periods brought to me later, as well as the entire twenty-four hours' quantity, after diets rich in carbohydrates, I could not find any increase of hexose, but, on the contrary, only occasional traces of it; nor did the pentose seem to be notably increased after he had eaten many cherries (kirschen)."

The diagnosis of essential pentosuria is established by the persistence of the pentose excretion and by the absence of other symptoms.

The chief importance of this condition at present, apart from the interesting questions in physiological chemistry to which it gives rise, is its liability to be mistaken for diabetes mellitus, or, at all events, for glycosuria. Indeed, most of the cases hitherto recorded have been so mistaken until coming under the care of a physician familiar with the fact that pentose may appear in the urine, when the diagnosis has been corrected.

Pentosuria is apparently an intractable condition, but occasions very little inconvenience, and, so far as yet appears, is devoid of danger to life. About the worst thing that can happen to the patient is to have the condition mistaken for glycosuria and to be restricted in diet accordingly. This is very likely to cause loss of strength as well as of flesh. When, however, the true nature of the case is recognized and a diet properly adapted to the individual conditions instituted, the patient rapidly recovers from this loss and appears to be normal in every respect, except for the urinary findings. The only medicament which, from report, seems to influence the condition favorably is arsenic. In the case of my own patient no medication has as yet been employed.

No light is thrown upon the metabolic fault concerned in the production of pentosuria by the habits, age, sex, vocation, nationality, or social and climatic environments of the patients as thus far recorded. Their ages vary from twenty to sixty-five years; they are of both sexes (although at first only males were reported), and their occupations, birthplaces, and environments have been as little similar as banking and farming; idling and practising law; wealth and poverty; Germany, Norway, Italy, and the Eastern and middle Western regions of the United States. Some of them have been morphine takers, some cocaine users, some neurasthenics. Two have been vegetarians. Quite a few cases have been observed in brothers or in sisters, or in brother and sister; so that there seems to be some indication of a family tendency.

As the pentose continues to be excreted, even when the patients

are put upon exclusive milk diet, and rarely seems to be increased notably, even by a diet of pancreas or pears, it is somewhat difficult to attribute the excretion of pentose to failure in assimilation of foodstuffs. The theory that pentosuria results from the breaking up of the pentose-proteid combinations of the body tissues has in its favor the discovery of arabinose in the blood of one or two patients; but against it, on the other hand, is the fact that the body pentose is l-xylose and the urinary pentose r-arabinose. Granting, however, that transformation of these isomers could be explained if we knew the intimate mechanism of the metabolic failure, there remains the still greater difficulty that the average daily urinary excretion in the cases thus far observed has been from 5 to 20 grams of pentose, whereas the entire body contains but about 10 grams. The problem, therefore, still awaits solution.

CHEMICAL EXAMINATION OF A SAMPLE OF URINE CONTAINING PENTOSE.[1]

By CHARLES H. LaWALL, Ph.M.

The urine, which had a specific gravity of 1023 and a yellow color, first attracted attention by the abnormal reaction produced when heated with Fehling's solution, which was not reduced to copper oxide, as is the case when the ordinary carbohydrates are present, but which produced a characteristic greenish turbidity and eventually a yellow precipitate. The fermentation test gave negative results, while a pronounced reduction was obtained by means of Boettger's test with bismuth subnitrate and solution of potassium hydroxide. A more extended examination, therefore, seemed desirable, and about a pint of the urine was furnished, with a request for an exhaustive investigation.

The first test applied was the alphanaphthol test, which is a group test for carbohydrates in general. It is applied by adding to a suspected sample of urine a few drops of a 10 per cent. alcoholic solution of alphanaphthol and then superimposing this liquid upon concentrated sulphuric acid. In the presence of any carbohydrate a violet zone is produced. This test resulted positively.

The Fehling test was then applied, with the result as previously stated. The reaction showed a greenish turbidity, which was succeeded by a yellowish precipitate, wholly unlike the normal copper reduction.

The Boettger test, with bismuth subnitrate and solution of

[1] Read May 5, 1909.

potassium hydroxide, showed a marked reduction to the dark colored metallic bismuth.

The indigo carmine test for dextrose gave negative results.

A fermentation tube showed no evolution of CO_2 after twenty-four hours.

A polariscopic examination of the sample showed that it was optically inactive.

The phenylhydrazine test was then applied as follows: A clean, dry, six-inch test-tube was filled to the depth of one-half inch with phenylhydrazine hydrochloride, one-half inch of dried sodium acetate was added, and the tube filled to half its capacity with the urine and immersed in a bath of boiling water for two hours. Upon cooling the contents of the tube a voluminous deposit of yellow crystals took place, which, when examined microscopically were found to be in stellate tufts of acicular crystals, resembling somewhat the groups produced by dextrose or levulose, but different in the character of the individual crystals, which seemed to be more slender in proportion to their length.

Several additional tubes of the crystals were prepared in a similar manner and some of the crystals were collected and purified by recrystallization. During this purification it was noticed that the crystals were much more soluble in hot water than is the case with ordinary dextrosazone. The purified crystals were found to have a melting point of 157° C. This corresponds very closely to the melting point of pentosazone, which was found by Salkowski and Jastrowitz to have a melting point of 166° to 168° C. when pure, but from 156° to 160° C. when obtained from urine. The melting point of dextrosazone (and levulosazone) is 204° to 205° C.

Several subsequent experiments upon fresh samples of material confirmed the melting point of the crystals, and the various specific tests for pentose were applied. Tollen's test, which is carried out by heating a solution of phloroglucin in hydrochloric acid and adding to the hot solution a small quantity of the urine, continuing the heat upon a water bath for some time, gave positive results in the shape of a cherry red liquid which became cloudy upon cooling.

As glycuronic acid also responds to this test, further confirma-

tion was obtained by applying the orcin-hydrochloric acid test, which is carried out similarly to the one previously described, using orcin instead of phloroglucin. In the presence of pentose a bluish green color is developed, which is dissolved out by shaking with amyl alcohol. Positive results being obtained by this test, thus negativing the presence of glycuronic acid, there seems to be no further doubt that there is exhibited in this sample of urine a well-developed case of pentosuria, as precisely the same results as above described were obtained in a specimen of urine from the same individual examined eleven months after the first report.

DISCUSSION.

Mr. Charles H. La Wall: I have prepared a number of tubes illustrating some of the conditions described by Dr. Cohen and showing the tests for the presence of pentosazone. The reaction by Fehling's test, as explained by Dr. Cohen, is peculiar, and it cannot be shown in a cold tube with good effect. It is of a greenish-yellow color. The after effect is to precipitate and leave an amber-colored condition, entirely different from the bright red.

The Boettger test is positive, showing a reduction to a grayish metallic condition. The indigo test was absolutely negative and the optical activity was zero except in the first instance.

Among the specific tests for pentosazone, the first to be applied is the test given as Tollen's test with phloroglucin and hydrochloric acid. The solution when boiled gives a cherry red reaction. This reaction was obtained positively. It is indicative of pentosazone, not conclusive, because the same reaction is given by glycuronic acid. The orcin test is a test made by saturating hydrochloric acid with the organic principle known as orcin and boiling this solution with a small quantity of the urine, whereby a greenish-blue condition is produced. This bluish color is capable of being removed by shaking with amyl alcohol. This test indicates pretty conclusively the presence of pentosazone, but it remains for the phenylhydrazine test and the preparation of the pentosazone crystals to make it positive. In our examination crystals were found conforming in their appearance to the crystals produced by dextrose, but differing materially in the melting point, which is 157° C. instead of 210° C. These crystals have been mounted and can be examined microscopically.

Dr. Cohen, closing: I believe these cases are much more common than the records indicate. I have no doubt that I, myself, have seen them without recognizing them. In looking over my records I find cases of abnormal reaction to Fehling's test, and I suppose that if these cases had been investigated in the same manner as was this one, doubtless in some I should have found pentosuria present.

SURGERY OF THE STOMACH.[1]

By JOHN B. DEAVER, M.D., LL.D.

The better interpretation of the early symptoms of upper abdominal disease, which I believe exists today, has encouraged me to read this paper, which I hope will have a slight influence at least in furthering the interest now being taken in the subject. I do not expect that all I have to say will be indorsed by everyone present. I am, nevertheless, of the opinion that my position in this matter, made strong as it is by many operations upon the abdomen of patients whose symptoms were those chiefly styled heretofore indigestion, is correct. Feeling as I do, I would not be true to myself did I not speak as I will this evening.

Today the chief problems of surgery lie in a region which may be covered by the palm of the hand placed on the epigastrium. Here we find, closely grouped, organs of the first importance, in digestion, and subject to a variety of diseases, functional and organic, which tax our diagnostic powers and our therapeutic resources to the utmost. The chief offenders of the lower abdomen, the appendix and the Fallopian tubes, are relatively remote from sources of confusion, their pathology chiefly that of inflammation, their symptomatology fairly definite, their position more accessible, and their functions being less essential, treatment was simplified by the simple and easy expedient of removal of the offending member in most cases.

Following the elucidation of these problems, the gall-bladder, that other chief focus of intraperitoneal infection, was energetically

[1] Read May 5, 1909.

attacked, and the surgery of the biliary apparatus today is resting fairly quietly on well-established principles and methods of procedure.

Next the searchlight was turned on the stomach and duodenum, and more recently the pancreas has been dragged forth from its modest retroperitoneal retirement and subjected to scrutiny. The stomach and first part of the duodenum, which must be considered with it from a functional and pathological standpoint, afforded the surgeon new and unusual difficulties, and he is still engaged in masticating this *pièce de résistance.*

I am asked to discuss "Modern Surgery of the Stomach." As a matter of fact, all surgery of the stomach is modern. Its beginnings do not carry us back thirty years, and the first tentative and hesitating procedures were carried out only in the presence of great emergencies. Only in the last ten or fifteen years has there been anything like a general movement to extend the therapeutic limits of the scalpel in the various ailments to which the stomach is subject.

For many years it has been well known that the chief organic diseases of the stomach are ulcer and cancer, and the earliest surgery of the stomach was directed toward those conditions. In 1880 von Mikulicz first sutured a perforated gastric ulcer, but his patient died. The following year Rydygier successfully excised an ulcer, and Wölfler performed the first gastro-enterostomy for the relief of pyloric stenosis.

These operations and their subsequent amplification and improvements have been called forth by the common knowledge that in these anatomicopathological alterations of the stomach expectant methods and all the assistance of drugs and hygiene fail to work a cure. Autopsies on the living have taught us much concerning the pathology of these persistent afflictions of the stomach and thrown light upon the treatment.

Of all the diseases of the stomach, ulcer is the most important. It is not so frequent, perhaps, as the slight functional disturbances from which few escape, but it is vastly more serious. It is not so uniformly deadly as cancer, but it is vastly more common,

and, moreover, in a large percentage of cases, is credited with being the starting point of the malignant change. Graham, in 145 cases of gastric carcinoma in the Mayos' clinic, obtained an antecedent history indicative of ulcer in 60 per cent.

That gastric ulcer is a more common affection than the clinician suspects is not difficult to prove. As long ago as 1885 Welch, in his masterly article in Pepper's *System*, showed that approximately 5 per cent. of mankind suffered at some time from this condition, as shown by the presence of open or cicatrized ulcers found at autopsy. Could we venture to suggest that some ulcers leave no scar apparent to the pathologist's eye?

Ulcers in the first part of the duodenum, which form, in the Mayos' experience, 40 per cent. of all ulcers of the stomach and duodenum taken together, should be considered clinically in this connection. Doubtless many duodenal ulcers have already been counted in the statistics of gastric ulcer, owing to their intimate relation to the pyloric ring, but certainly some duodenal ulcers were not so included, and if we may add these two groups to the already stated percentage it can hardly fail to swell materially the estimate. But even adhering to the original figure of Welch, can we say that, of every twenty individuals, we can find one in whom at some time ulcer of the stomach or first part of the duodenum has been diagnosticated?

It is apparent that our average will fall far short of this. Evidently, then, the disease gives no symptoms in many cases, or they fail of recognition. It is repugnant to our ideas of an ulcerative process sufficient to give macroscopic evidence of its presence, even long after healing, to suppose that it can exist without symptoms, and, moreover, in the presence of such a multitude of cases of "indigestion" in which no definite idea of the pathological basis is held, it would seem to be going rather far afield to ascribe these symptoms to undiscoverable causes and leave ulcer the symptomless wonder of the clinician.

It is plain that the symptomatology of this condition must be enlarged, that we must not hold a diagnosis contingent upon such conditions as pain of a certain type, occurring at a certain time,

with nausea and vomiting, hematemesis and melena. Osler says, "For months and years the patient has had dyspepsia, and the ulcer may not have been suspected until the occurrence of a sudden hemorrhage." The conviction that these dyspeptic symptoms should be correctly diagnosticated has been growing until we find a man of great experience in this disease, Mr. Moynihan, of Leeds, who says, "It is almost as reasonable to wait for hemorrhage before venturing to diagnosticate a duodenal ulcer as to include a ruptured perineum among the signs of pregnancy." And what is true of duodenal ulcer holds with equal force in ulcers of the stomach, though it must be said that in gastric ulcer hematemesis is relatively more frequent than in duodenal ulcer, just as melena is more frequent in the latter condition.

It should not be a cause for discouragement that we cannot as yet carve out a sufficiently definite symptom complex to enable us to recognize, with certainty, ulcer in its early and so-called latent stage, but rather an incentive to greater effort. It is necessary to keep ever before our minds that ulcer is vastly more frequent than our diagnosis would indicate; that we must, therefore, be treating many cases in a haphazard manner for dyspepsia who are really suffering from this condition, and by so doing, permitting a certain percentage to go on to perforation, hemorrhage, or the callous stage, which is so resistant even to palliative treatment, and inflicts so much misery upon the victim. These are considerations which are of more interest from a medical than from the strictly surgical aspect, and express my belief that ulcer in this situation, as elsewhere, is quite amenable to the ordinary principles of treatment by rest and protection.

That fact remains that those cases which come into prominence at the present time with a diagnosis made on the recognized principles are aggravated forms and present a very different prognosis from early ulcer.

Greenough and Joslin's excellent statistics concerning 187 cases of this condition treated by medical means in the Massachusetts General Hospital give an immediate mortality of 8 per cent., while 80 per cent. were discharged as cured or relieved.

After an average period of five years, of 114 patients who could be traced, it was found that just half had relapsed and 15 additional cases had died of gastric disease, making a total of 20 per cent. of deaths within the five years from the disease, certainly not a reassuring prognosis for those patients upon whom a diagnosis of ulcer is made by present criteria. Bulstrode's analysis of 500 cases admitted to the London Hospital for gastric ulcer between 1897 and 1902 showed 18 per cent. immediate mortality, of which 10 per cent. were from peritonitis, 2.5 per cent. from hematemesis, and 5.5 per cent. from other causes. He estimated recurrences after "medical cures" as at least 42 per cent.

The ulcer of indefinite and minor symptoms is by no means free from danger, as it is not so uncommon for a perforation or severe hemorrhage to drop "from the blue," but I wish especially at this time to emphasize the gravity of all cases which come within our clinical ken.

If we *will* shut our eyes to the numerous mild and early cases we must be willing to act energetically when a percentage of these cases, whether by reason of the severity of the process, the poor resistance of the tissues, or by neglect of treatment, enter the easily recognizable and especially dangerous stage. In this stage the estimates of mortality range from 10 per cent. by Lebert to 50 per cent. by Brinton in the case of gastric ulcer, while that of duodenal ulcer, being a more dangerous condition by reason of the more delicate structure and unprotected situation of its wall, is somewhat higher. Statistics in this connection, as elsewhere, are apt to be misleading, but it is plain that an ulcer which can be diagnosticated is a condition in which one should not temporize, but rather respond with the best means at our disposal. The indication is rest for the part, and not only rest, but a long rest. This factor of time is what removes most of these cases from the sphere of the medical man to that of the surgeon. It has been abundantly proved that it is impossible to provide rest by medical means for a sufficient time to permit a cure in the majority of cases.

Gastric drainage is the solution, and the credit for suggesting the principle belongs to Doyen, who proposed it in 1893. Since

then its efficiency has been amply demonstrated, and eminent surgeons are a unit on the remarkable results obtained in this way. Kocher, a man of the keenest scientific habit of mind and conservatism of judgment, voices the general sentiment when he says:

"The majority of practitioners do not sufficiently realize what brilliant results are to be obtained by operative means in chronic affections of the stomach commonly known as gastric catarrh.

"Not only can the numerous dangers of ulcerating affections of the stomach, such as hemorrhage, perforation, transition into cancer, be prevented, but the disease and its results may be so rapidly and certainly cured that the medical treatment of obstinate cases must be put in the background.

"The pain in the stomach disappears immediately after the operation. This is the invariable rule. The patient does not require to pay any further attention to the nature of his food.

"The vomiting disappears.

"The bowels become regular.

"Repeated investigation of the gastric contents shows that there is a progressive improvement in the process of digestion; hyperacidity diminishes; if too little acid is present, it becomes increased."

This sounds too good to be true, but it has been repeatedly observed. What is the operative mortality of the simple procedure of gastro-enterostomy required to work these wonders? In the best hands from 3 to less than 1 per cent., and constantly diminishing. Compare this with the 8 per cent. immediate mortality above quoted and the additional 12 per cent. to be added in the next five years. And throw into the balance the large percentage of recurrences under medical treatment. Opposed to these figures are the results quoted by seven eminent surgeons in nearly 1000 cases of from 73 to 93 per cent. of cures, and the remainder about equally divided between relieved and unimproved. Really these are wonderful results when one considers that only the most severe cases have been turned over to the surgeon.

Gastro-enterostomy then is the treatment of choice in these

cases of simple, chronic, persistent, symptom-giving ulcers of the stomach and duodenum.

The complications of ulcer are various. A case tided over medically is not even assured of life, albeit with more or less severe dyspepsia. There is no security against perforation which may occur in an acute form freely into the abdominal cavity, and in a subacute form where the slowness of the process has given time for perigastric adhesions to limit more or less the results of the perforation. In this case we may find adhesions, subdiaphragmatic abscess, or localized collections of pus elsewhere in the abdomen. Chronic perforation is the term applied to that condition in which extensive perigastric inflammation has provided the ulcer with a new bed without the stomach by the time the serosa is penetrated, so that dissemination of infection within the abdomen is prevented. Slow sepsis, distortion of the stomach, and hemorrhage from an eroded artery are here the dangers.

The acute form requires instant diagnosis and prompt surgical intervention. The ulcer must be closed and appropriate drainage instituted, while if the patient's condition warrants the procedure, and it usually does, I am accustomed to do a gastro-enterostomy to promote healing and provide against later complications from the same source.

In the subacute and chronic forms of perforation the time allowed for action is increased, but the indications for surgery are just as evident.

The danger of hemorrhage is ever associated with the presence of an open ulcer. It may be slight capillary oozing or more free bleeding from venous or arterial trunks. Erosion of a vessel in the wall of an old indurated ulcer is apt to be fatal on account of the fact that the vessel walls are held as by a vise preventing collapse or retraction and clot formation. I have recently observed a fatal case of this sort from erosion of the coronary artery.

Chronic recurring hemorrhages, whether occult or macroscopic, are an absolute indication for operation.

The very processes of spontaneous cure bring with them their special dangers. Cicatrization of an ulcer at the pylorus is a not

infrequent cause of stenosis with subsequent dilatation. Occasionally tetany develops in cases of marked gastrectasis. These conditions are readily relieved by a gastro-entero-anastomosis, and afford an example of the most brilliant cures we have the power to bestow.

If the ulcer be not at the pylorus, or if it has given rise to perigastric adhesions, distortion of the stomach may follow, one of the most typical forms being the familiar hour-glass stomach.

The method of procedure in these cases will be governed by the anatomical conditions, but in general consists of release of embarrassing adhesions and provisions for drainage of insufficiently drained pouches of the stomach. Occasionally it may be desirable to resect the diseased area and reunite. In a case which exhibits only a moderate degree of contraction, with a relatively normal wall, a simple gastroplasty might suffice.

Where there is any doubt as to the provision of proper drainage for the proximal pouch by this method, as is usually the case, a gastrogastrostomy uniting the two pouches should be done, and is best supplemented by a gastro-enterostomy. Resection as an operation of higher mortality should be reserved for those cases in which the character of the gastric induration excites suspicion of carcinoma.

Definite gastric diverticula are rare, and due in most instances to the traction of perigastric adhesions aided by intragastric pressure. Excision has been successfully done in two cases. These cases both presented a firm, painful tumor in the epigastrium adherent to the anterior abdominal wall, and gave histories indicative of chronic ulceration. Not enough cases have as yet been collected to generalize on the question of treatment. Doubtless in simpler cases a drainage operation will be found sufficient after release of adhesions.

In dealing with uncomplicated ulcer, where it is desirable simply to secure drainage, a gastro-enterostomy is satisfactory and the most generally applicable procedure. The posterior no-loop or very short method, uniting the most dependent portion of the stomach with the jejunum at its origin behind the peritoneum, has

proved the best in our hands, as in those of most other surgeons. I have not seen a case of vicious circle follow one of these operations since using this method.

In regard to the direction of the incision in the stomach, we may take counsel of function or of anatomical detail. I have usually followed the method of Petersen and made the opening inclined slightly to the right from above downward, suturing the proximal portion of the jejunum to the upper angle. This creates a condition which more nearly approaches the normal peristaltic direction. Of late, however, I have also made the opening incline to the patient's left, as advised by Mayo, to permit a more normal situation of the jejunum, with equally good results.

In case extensive disease of the posterior wall, or adhesions or other abnormality prevent a posterior anastomosis, an anterior gastro-enterostomy may be done. In this case I think it wise to do an entero-enterostomy between the ascending and descending loops, as it adds little to the length or gravity of the operation and may ward off the dreaded vicious circle. Should such a complication arise after the entero-enterostomy, however, I believe it would then be proper to tie off the pylorus, and as a final step to ligate the afferent loop between the entero-enterostomy and the gastro-enterostomy openings.

In cases of simple stenosis of the pylorus, in which the tonus of the stomach has not been lost, and the pyloric tissues are still relatively delicate and healthy, a pyloroplasty after the method of Finney would most nearly restore the anatomical relations of the parts, and is therefore to be preferred. In these cases also, however, a gastrojejunostomy seems to give as good a functional result and is associated with less risk. When the stomach wall is greatly distended or hypertrophied, I am inclined to believe that drainage from the most dependent portion of the stomach will give better functional results than widening of the pylorus, owing in the first instance to the frequent failure of a thin walled dilated stomach to recover its tonus, and in the second instance to a hypertrophic insufficiency such as we often see in greatly hypertrophied bladders.

Old indurated ulcers are often hard to distinguish from malignant change, and, indeed, it is well known that malignancy is not infrequently implanted on the edge of such a process. In a doubtful case excision is advisable. As these ulcers are practically always in the pyloric portion of the stomach, they lend themselves readily to the method of pyloroplasty which I shall mention in speaking of the treatment of cancer, and this complete resection is, I believe, preferable to local excision and gastrorrhaphy. A calloused ulcer in an unfavorable location for resection or where there is no danger of interfering with drainage may properly be excised.

Finally, I advocate caution in the diet after operation. These patients are usually so much relieved that in their enthusiasm they neglect ordinary precautions. Thus, they may defeat our purpose of procuring rest for the diseased area. The best results to be obtained by medical treatment are after and not before operation. I may say here that I have in several cases operated on a diagnosis of ulcer and found only perigastric adhesions, release of which has relieved the symptoms.

Of all organs, the stomach is affected by cancer next in frequency to the uterus. Its pathology is well known, and in no disease has a clearer text-book picture been drawn than in this. The student with his general symptoms, local symptoms, local examination, and stomach contents well in hand can generally make an antemortem diagnosis. But nowhere do we see the need of a professor of practical medicine in our schools more than in connection with this same disease. The abdominal surgeon to whom the profession looks for aid in these cases has cried out until he is hoarse that cachexia, hematemesis, mass, enlarged liver, and anacidity are symptoms not of cancer but of approaching dissolution, and still we talk of loss of weight, anemia, palpable tumors, and stomach contents, and the early symptoms are, if mentioned at all, dumped in with the late, and never a text-book to devote a paragraph to symptoms we may get while the disease is yet local and curable. It is clear that the reason why carcinoma in this situation is relatively so much more deadly than carcinoma of the lip or breast is simply that an early diagnosis by direct

inspection and palpation cannot be made in cancer of the stomach without the formality of an operation. Hence the importance of acting on suspicion. There is but little use of the practitioner bothering his head about a diagnosis if he insists on certainty. By the time he is certain of his diagnosis, he is also certain of the prognosis. Therefore, I am inclined to say that a positive diagnosis is a disgrace to the physician in attendance, providing he has been following the case for some weeks or months.

The latest device which has been invented to defer operation until it is too late is gastric analysis. Ewald, who has had a test meal named after him, and was the first to announce the absence of free hydrochloric acid in the gastric contents in this condition, states in italics in his book that "the presence of free hydrochloric acid in the stomach contents points with very great probability against the existence of carcinoma." What words can I use sufficiently strong to denounce this vicious falsehood? Righteous indignation should permit the use of a "shorter uglier word" in speaking of a statement that takes from the unfortunate victim of the disease his one chance of cure, early recognition. I have had for some years routine examination of the stomach contents made in all cases of upper abdominal disease in which the stomach may be affected, including disease of the gall-bladder. At first hopeful of deriving assistance from this source, my disappointments were so frequent and great that I have come to place no reliance on the method. Still I have had them continued as a matter of record, and for the purpose of this article I had tabulated the last fifty examinations that were subsequently controlled by operation. The conclusions, not to weary you with figures, are these:

Anacidity is not infrequent in disease other than that of the stomach, *e. g.*, in 5 cases of 25 of disease of the gall-bladder.

In early carcinoma the acidity is but slightly altered.

In late inoperable carcinoma normal or but slightly subnormal acidity may occur.

Anacidity has almost invariably gone hand in hand with an extensive inoperable growth. Surely the clinician who wishes

to be "writ as one who loves his fellow-man" can have little use for this reaction in the diagnosis of cancer.

Lactic acid does not appear until acidity is greatly diminished or absent, therefore practical workers can lighten the boat of this weight.

The ferments are usually the last to disappear. Throw them overboard.

Blood, even occult blood, indicates ulceration. How often does a carcinoma ulcerate in its early stages?

The Oppler-Boas bacillus is extremely inconsistent, and occurs only in the late stages of stasis and subacidity. It may be found in conditions of stasis and fermentations from benign causes, and has no essential relation to malignant disease.

The *x*-rays give no aid of any moment. We can determine with considerable accuracy the position, shape, size, and motor power of the stomach by other simple means. The *x*-rays cannot hope to do more, and, moreover, they often introduce sources of error through difficulties in interpretation. Where surgery will do most, *x*-rays will do the least.

What have we left? We have a patient approaching or past middle life who either suddenly or on top of previous gastric disturbances finds that his digestion is getting rapidly worse. He has little inclination to eat; some articles of food, oftenest meat, but not invariably so, excite disgust. He feels a certain languor and lack of vigor. Eructations of gas, regurgitation, and a slight feeling of discomfort in the epigastrium or left hypochondrium may or may not be present. He begins to lose weight. In the absence of a very definite cause outside the stomach which could give rise to such symptoms, this man should have his stomach inspected directly. This will be at times needless. Again, other disease than carcinoma will be found, but in a large percentage of these cases we will be rewarded by finding early neoplasm curable by extirpation.

In rare cases of primary involvement of the orifices the diagnosis will be easy while the disease is still local. In most cases the diagnosis can as yet be only presumptive, and he who prefers

to risk his patient's life by waiting rather than his reputation on an exploratory operation may be a successful but not a high-minded practitioner.

The ideal treatment for cancer is complete excision. In the vast majority of cases the disease arises in the pyloric or grinding portion of the stomach, its location thus agreeing with that of ulcer. By a fortunate arrangement of the lymphatics it does not tend to spread to the fundus. The glands of the lesser curvature are early involved, as is the adjacent gastrohepatic or gastrocolic omentum. By a wide excision, then, embracing these structures we hope to circumvent the disease in the early stages.

The method I employ is essentially the Billroth No. 2, and consists of removal of that part of the stomach lying between the first portion of the duodenum and the Mikulicz-Hartmann line, which is an imaginary perpendicular dropped from the cardiac orifice to the greater curvature. The cut ends of the stomach and duodenum are closed and a posterior gastro-enterostomy done in the usual manner. Various modifications are occasionally necessitated by mechanical conditions. Thus, where the chief operative difficulty is about the duodenum, by reason of immobility or adhesions, I sometimes find it preferable to make the excision from above downward, first dividing the stomach instead of the duodenum, as usually recommended. The amount of stomach which it seems wise to remove will govern the length of the loop and location of the gastro-enterostomy opening. For this reason I do not believe it wise to do the anastomosis before the excision, and for the same reason I would prefer to perform the whole operation in one sitting, rather than do the gastro-enterostomy first and wait for improvement before attempting resection. I reserve this last procedure for those cases in which an early stenosis of the pylorus has caused such a serious condition of starvation that I fear for the life of my patient.

It is sometimes wise to excise somewhat more of the stomach than has just been indicated. Such an operation has been distinguished by the term subtotal gastrectomy.

A complete gastrectomy is rarely indicated. Such extensive

invasion of the gastric wall as to make this operation requisite will usually be found to be accompanied by so many perigastric adhesions or by such obvious metastases as to render useless any but a palliative operation. On the 28th of last month I performed such an operation on a patient whose pyloric portion I had resected two years previously for carcinoma, which was then quite extensive and situated chiefly on the lesser curvature. For a year following this operation he had enjoyed excellent health. During the year following he had been going down hill again, and the symptoms on this admission were definitely those of recurrence.

He had derived so much benefit from his previous operation that he was anxious for another attempt at cure. Accordingly, though without much hope of being able to accomplish anything, I made an exploration. The fundus of the stomach was extensively diseased and there were numerous adhesions. In the absence of demonstrable metastasis I determined to resect the remainder of the stomach, which was done. An attempt to unite the esophagus and jejunum by a Murphy button proved futile owing to the retraction upward of the severed esophagus and consequent torsion. I therefore anastomosed by suture. Fearing accident to this esophagojejunostomy, I supplemented the operation by a jejunostomy. So far the patient has done very well, but it is hardly to be expected that he will get a permanent cure.

The surgical treatment of advanced carcinoma, in which it is hopeless to get beyond the growth, is a very unsatisfactory part of surgery. The most frequent call for a palliative operation comes from pyloric stenosis with the distressing symptom of retention. A gastro-enterostomy in such cases will often give marked temporary relief, and on the average has been shown to add about three months to the expectation of life.

In obstruction at the cardiac orifice death from starvation may be prevented by a gastrostomy, for which there are several satisfactory operations. The methods of Senn, Witzel, and Koder are simple, effective, and yield probably equally good results, though my preference is indicated by the order. So long as a patient can swallow liquids this operation is not indicated.

A jejunostomy or duodenostomy may occasionally be advantageously done in cases of marked disease of the stomach wall rendering a gastrostomy difficult of performance. It will rarely be necessary or advisable, however, to employ these operations.

In all these palliative operations there is danger that the patient may become bedridden from the effect even of an exploration, and it is imperative to accomplish what is necessary with the least manipulation and in the shortest time possible. Then they should be gotten out of bed in four or five days.

In the future I hope we will have fewer explorations on cases with a positive diagnosis to see whether something can be done, a hope practically always illusory, and more explorations in suspicious cases while there is yet a chance of cure.

In the prosecution of this work it is necessary to have constantly in mind those minor and functional disorders of the stomach, than which nothing has done more to cast doubt upon gastric surgery. Ill-advised operations, where there is no organic disease or mechanical difficulty, can hardly be expected to result otherwise than in failure. It is true that we have a surgeon of recognized ability in New York advocating operation as a method of producing a profound effect upon the mind in cases of neurosis. But I am unwilling to lend surgery to the purpose of psychotherapy, and regard such subjects as proper material for the internist with neurological propensities. Such cases may be hard to differentiate, but, as I have recently pointed out, they usually show other neurotic stigmata, often suffer from overwork or worry, with obsessions of various kinds, and show a peculiar variability of symptoms, being remarkably susceptible to any change in treatment and hopeful suggestion. It is in these cases that we do find a use for our laboratory methods, since they are usually chronic cases in which we would expect to find marked departure from the normal motor and secretory functions in case of organic disease, but in the existing condition may find no abnormalities. Such cases are better untouched, or if explored under a misconception no operative procedure should be done on the normal appearing stomach. I believe it is proper in this class of cases to make

ostentatious use of lavage, massage, electricity, or any agent likely to have a strong psychic effect.

Some of these cases need surgery, but not gastric surgery. It has been pointed out many times, and should be known, that a certain type of chronic appendicitis or of disease of the biliary apparatus or pancreas may give stomach symptoms so marked as to rule the picture. This is often due to the condition known as pylorospasm, which, if ever primary, is practically always secondary to some other lesion of the alimentary tract or its related structures. It consists in the reflex closure of the pyloric sphincter, with consequent retention of gastric contents and motor and secretory disturbances. Stasis, fermentation, and perhaps dilatation may follow, and these symptoms of gastric indigestion may so distract attention from the true excitant of the reflex that it easily remains undiscovered. Hence the importance of considering all the abdominal organs in dyspepsia. The treatment is accordingly that of the underlying pathology. Somewhat analogous to pylorospasm is the condition known as cardiospasm, in which there is more or less obstruction to the food by spastic contraction of the cardiac sphincter. Mild cases probably often pass unperceived. In more severe cases interference with nutrition may be serious. Thorough trial of bougies and dilators passed down the esophagus should first be made. If these measures fail to relieve, much can be done by opening the stomach and divulsing the sphincter. A fair number of cures by this method are on record.

Gastroptosis is usually associated with general visceroptosis, and an operation on any one of the displaced viscera promises little. Simple gastroptosis doubtless does occur, and in such cases, provided symptoms are severe, one of the proposed operations, such as taking up the slack in the gastrohepatic omentum, may be done, but I may say that, in general, I am not inclined to recommend operation in cases of ptosis, and certainly not until the effect of a properly fitting abdominal supporter, with general medical treatment, is tried.

There is one condition not associated with demonstrable organic

lesions of the stomach in which an operation may be serviceable and give truly brilliant results. This is the condition of gastrectasis, or dilatation of the stomach, in the presence of a patulous pylorus. My friend, Dr. Harvey Shoemaker, has often spoken to me of the excellent after results obtained in several patients of this class referred by him to me for operation.

The precise cause of this atonic condition we do not know. It is often associated with low states of health and disease of other organs, particularly within the abdomen. It can be demonstrated experimentally that the majority of sympathetic fibers supplying the stomach are inhibitory, and that stimulation causes relaxation and dilatation. This suggests a plausible etiology in reflex stimulation through the splanchnics from a more or less remote focus of disease, and this would correspond to our clinical findings of various abnormalities associated with this condition. Be that as it may, the stomach once distended beyond certain limits loses its power of elastic recoil, and to the original cause of dilatation there are soon added gastric stagnation, fermentation, and often a kinking at the pyloric outlet to interfere further with complete emptying of the organ. Thus, dilatation becomes permanently fastened to the subject, and with the digestive disturbances and secondary debility of nerve and function may remain as the sole legacy of the original condition. In such cases medical treatment has been given a thorough trial before I am willing to operate. In fact, to use a phrase of William Mayo in another connection, such a case should be operated upon after it has had nine medical cures. The best operation to secure efficient drainage is a posterior gastro-enterostomy done at the most dependent part of the stomach. A pyloroplasty is here of less value, since the motor function may have been so impaired as to be unable to empty the sagging pouch of the greater curvature, against the slight force of gravity even in the presence of a wide and non-resisting outlet.

Gastroplication, or the operation of reducing the size of the stomach by a series of pleats, is, I believe, less likely to be successful, though in this opinion I do not speak from personal experience.

It has never fallen to my lot to see a case of acute dilatation of the stomach such as are by no means uncommonly reported in the literature. After wondering at the strange immunity from the affection in a large service covering now many years, and the varied operations, mostly within the abdomen, I have come to the conclusion that the reason why we do not see them is by reason of the early and free use of the stomach tube in all cases which show accumulation of fluid or gas in the stomach. I have seen cases with massed flatulence, eructations, more or less vomiting, discomfort and distention of the upper abdomen so wonderfully relieved by the use of the tube that I have speculated on the probable outcome if the accumulated fluid and gas were not so removed. It is my firm belief that a percentage of these cases would have perished from so-called acute dilatation.

The treatment of this affection is, then, in my opinion, early recognition of the onset and prevention by means of lavage. Elevation of the foot of the bed, preventing sagging downward of the stomach and the obstruction of the duodenum by the root of the mesentery, as the intestines prolapse downward, may be valuable adjuncts. This treatment would apply as well to those cases occurring as a primary affection or as a complication in other than operative conditions. There is a form of gastric dilatation encountered in infants as a result of stenosis of the pylorus. Whether this is due to a congenital abnormality, to hypertrophy, or to spasm is as yet not determined. The clinical features have suggested the term hyperemesis lactantium. It is recognizable by the vomiting which begins usually about the first week, by the obstinate constipation and progressive emaciation, and by the formation of epigastric tumor with visible peristalsis. Severity of symptoms, of course, varies with the degree of obstruction. It is advisable to try all medical means of relief possible without permitting the patient to become moribund from inanition. When it is evident that palliative measures are unsuccessful, operation promises much. Of 152 cases of operation reported, there were 79 recoveries. Analysis of the results as well as our personal feeling would indicate a preference for some form of pyloroplasty as the best procedure.

It is impossible to cover this whole field in such a short space of time. I have, however, touched upon the most important subjects and confined myself strictly to practical aspects.

The chief point to emphasize, however, in all this subject still is that we must not allow the frequency of minor and functional disorders to divert our attention from the common occurrence and serious nature of ulcer and cancer. Ten years ago gastric surgery was far behind diagnosis. Today it is just as far ahead, and we wait, perhaps impatiently, for the internist to come abreast.

DISCUSSION.

Dr. John H. Musser: It would seem to me rather better, perhaps, for some of my younger friends, who are not quite so conservative as I am, to open the discussion. I am very glad to discuss, however, certain features of the paper, provided we understand clearly that we are discussing a paper on the rational basis for the surgical treatment of certain forms of symptomatic indigestion. If, therefore, one remembers that we are speaking of a surgical treatment of symptomatic indigestion, no exception can be taken to the paper so ably and forcefully presented by Dr. Deaver. I should like to say a word in regard to that form of indigestion which I think is very frequently overlooked, and which might give rise to both acute and chronic symptoms, namely, cases secondary to adhesions about the pylorus, the result either of a previous pancreatitis, a cholecystitis, or duodenal ulcer. I have had quite a number of such cases operated upon, and practically the symptoms were those of pyloric obstruction, such obstruction being only relative rather than actual.

Of course, there are, too, as Dr. Deaver has pointed out, innumerable cases of indigestion that do not have these surgical indications; such as indigestion in the course of chronic cardiac disease, chronic nephritis, the indigestion of anemia, a number of underlying conditions or of functional conditions similar to the indigestion that arises from dietetic errors, and, perhaps more frequently one sees the indigestion the result of poor mastication and poor teeth than any other form, an indigestion which under such circumstances leads to a chronic gastritis and is the most obstinate form we have to deal with, because there develops an associate persistent chronic anemia.

While it is quite proper to advise surgical procedures in many instances, there is a very large number of cases that we cannot expect to benefit by surgery, even though they are symptomatic cases of indigestion.

When the call is loud for surgery in gastric ulcer we must remember that one does not have many cases of death from hemorrhage or perforating gastric ulcer. Once in a year or two in the large hospitals there may be a death due

to this cause, but the mortality is not as great as many statements lead us to believe. If we are going to operate so extensively in these affections, surgeons of any degree of experience will be operating, and therefore, if we balance up the results of surgical treatment with medicinal treatment, I do not know but that the latter would count with a little better percentage than the former. I do not say this with the idea of opposing operation in such cases as suggested by Dr. Deaver. I urge operation in many instances. In the case of a chronically inflamed appendix, where there are symptoms making life unendurable, operation is indicated. I do not think, however, that we should rush along and give the impression that we are doing these things all the time, and so strongly indorse operative treatment that anyone who wishes to operate will feel privileged.

I have no other criticism to make of Dr. Deaver's paper, except in regard to his suggestion as to the treatment of gastric diseases by eight or ten remedies in a way that would do discredit to the profession.

Dr. Joseph Sailer: It is, I believe, commonly agreed that the basis of all therapeutics, whether medical or surgical, is an accurate diagnosis, and until this is obtained no intelligent treatment can be employed. The symptoms of chronic indigestion, of chronic gastritis, or whatever name is selected for them, may depend upon a great variety of conditions, as tuberculous valvular heart disease, acute intracranial conditions, or some abdominal condition not directly connected with the stomach, but which can be relieved by surgical operation. I am not in favor of operations in these cases until there is some definite reason for it other than the failure of medical treatment. In the first place, there are cases in which chronic conditions are found in the abdominal cavity, and which, for some reason, operation fails to relieve, although apparently there is every reason for expecting surgical measures to be successful. I have under my care several patients who have had operations for apparently simple conditions and yet are worse than they were before the operation was performed, and in every instance these operations were done by competent surgeons. It is possible that one explanation for these cases has been the factor of which I spoke in the beginning, "inaccurate diagnosis." One thing having been found, it is assumed that it explains all the symptoms, and consequently another and perhaps more important factor has been overlooked either in the preliminary study or at the time of the operation, and this is particularly likely to be the case if some definite lesion has been found; secondly, the exploratory operation is often futile. I do not mean merely that inoperable conditions are found. This is no reason why exploration should not be done; rather it is desirable to give a patient with a hopeless disease even the remote chance. I know of a number of instances in which only a painstaking dissection at the autopsy, such as could not possibly have been performed during life, revealed the exact nature of the lesion. In other cases it is difficult to determine what a lesion

is until there has been at least a microscopic examination, possibly aided by cultures. I have often been puzzled myself, as a pathologist, and have seen as good a man as Flexner in doubt regarding abdominal conditions until further laboratory-studies had determined their true nature. Particularly in cases of gastric ulcer it is difficult to decide in many cases at the time of operation. I remember one instance in which operation was performed for repeated hematemesis. A very thorough examination of the stomach failed to show any signs of ulceration, although previously, localized tenderness, persistent occult blood in the feces, and all the other characteristic symptoms were present.

A great deal of work has been done, and is being done, to increase the accuracy of diagnosis in abdominal conditions. At the present moment this is particularly true of pancreatic disease, and I must say that, in my opinion, the liver is being to a certain extent neglected. Some of the work on pancreatic disease is suggestive, and some is not only valueless but also in some respects, misleading. Take, for example, the Cammidge reaction. No doubt it has been found present in other conditions than pancreatitis, but the improved reaction is undoubtedly present in the majority of cases of chronic pancreatitis, but in one case under my care it was sometimes present and sometimes absent.

As Dr. Musser has said, there are various kinds of surgeons, and, as Dr. Deaver has replied, there are also skilled and incompetent physicians; but I believe there are few responsible medical men who do not at the present day exhaust all the measures at their command for the purpose of accurately diagnosticating their cases.

Dr. James E. Talley: The diagnosis of morbid conditions in the upper abdomen today is about where appendicitis was fifteen years ago. I interested myself to look over my cases of gastric ulcer, with complications, seen in the last few years. To one that I could get to a surgeon, half a dozen absolutely refused to have anything done. I recall a girl with hemorrhage five years ago. So great is the pain after food that for five years she has eaten but two meals a day, and herself practises lavage two or three hours after meals. A woman, now of middle age, had her first hemorrhage in 1888. She has had recurring hemorrhage, many times every year since. She is in wretched health, is emaciated and weak, and in the last year, in addition to her hemorrhage, had an attack of cholecystitis; yet in spite of her double trouble I cannot get her to a surgeon. Another woman of middle life, with indurated ulcer and perigastritis on the anterior wall of the stomach, has in years become a confirmed neurasthenic, and finally developed mucous colitis. One man is the subject of large recurring intestinal hemorrhages, and another of gastrosuccorrhea. All of these cases are surgical cases, and within the next fifteen years people with similar complaints will have changed their attitude toward surgery as it has already changed in the matter of appendicitis.

Dr. Frederick P. Henry: There are several well-known facts which do not harmonize with the statement that most of the cases of so-called dyspepsia are due to organic disease of the stomach. One of these is the rarity with which signs of organic disease of that viscus are found at the autopsies of individuals in whom such disease had not been suspected; the second is the extraordinary prevalence of gastric disorder in people who may be fairly regarded as healthy. Forty or fifty years ago the American people were characterized as a "nation of dyspeptics." It seems hardly likely that the most energetic progressive people in the world were suffering to a wide extent from organic disease of the stomach. Of late years, with diminishing "dyspepsia," there is said to be an increase in the number of cases of organic gastric disease—a fact which seems opposed to Dr. Deaver's views.

I agree with Dr. Musser and Dr. Sailer in what they have said, but I go farther and consider that numerous cases of gastric disorder are purely functional, and that many more are due to catarrhal inflammation. What is more common in children than acute gastric catarrh?

I do not think that physicians in general are as careless in their diagnosis of gastric diseases as seems to be assumed. The first question which arises in the mind of the physician who is confronted with a case of persistent gastric disorder is, Have I to do with a case of functional or organic disease; and, if organic, is it amenable to surgical treatment?

Dr. Deaver, closing: I cannot take exception to anything that has been said except to the statements of my friend, Dr. Henry. I agree in detail with all that Dr. Musser, Dr. Sailer, and Dr. Talley have said. My paper did not include indigestion from causes other than disease of the abdominal viscera. Pyloric adhesions are not an uncommon cause of digestive disorder, as Dr. Musser has said. I have seen this particularly pronounced in cases of gallstone disease and after gall-bladder operations, such as cholecystectomy. Regarding the line of drugs which I mentioned; of course, they would not be given by any Philadelphia internist, but I regret to say that some of our stomach specialists in New York do give them.

Dr. Sailer has hit the nail on the head when he speaks of early diagnosis. The object of my paper was to urge exploratory operation, particularly in the presence of doubtful cases, and if it serves that purpose I shall be well rewarded. Dr. Sailer properly speaks of operations that have been performed and the patient no better off. I regret that I have performed operations of that kind. Having opened a belly and not found a lesion, the experienced surgeon should not attempt to do any operation with the hope of relieving the condition. Exploratory operation should not be done until every other diagnostic method has been employed; but the patient should not be treated for months and months before exploration is resorted to. It has been well said that there is only one way to diagnosticate gallstone disease, and that is

to know the pathological anatomy. And the only way to know the pathological anatomy is to stand at the operating table and study the pathology. My friend, Dr. Henry, speaks of not seeing these conditions at autopsy. We are not seeing them because surgeons are curing so many cases that they do not come to autopsy. I don't believe in catarrh of the stomach except from indigestible food, poisons, etc. If the condition is persistent the cause is outside the stomach.

TREATMENT OF TYPHOID FEVER BY THE MURPHY METHOD OF CONTINUOUS SALINE INSTILLATION.[1]

By DAVID RIESMAN, M.D.

I WISH to preface what I have to say about the Murphy treatment in typhoid fever with a few remarks on the pathogenesis of the disease. We are accustomed to attribute the symptoms of typhoid fever to the typhoid bacillus and to such lesions, produced by ulceration of the bloodvessels, by perforation, etc., as are the indirect result of its action. The general symptomatology of the disease—the fever, the cerebral symptoms, the altered metabolism, and the acute degenerations in the parenchyma of organs, are ascribed to a typhoid toxemia brought about by the entrance into the blood of the poison of the typhoid bacillus. Unlike the toxin of tetanus, this poison is not a secretory product of the organism, but is an endotoxin laked out of the bodies of dead bacteria. As this view of the pathogenesis of typhoid toxemia is the one almost universally accepted, it may be bold to question its correctness. But it seems to me that it is not a full and adequate explanation of the principal phenomena of the disease. There is another source of toxemia which the prevailing theory leaves out of account. I made mention of it in a paper published in 1899,[2] and in a discussion of Dr. Mallory's address on typhoid fever before the Pathological Society a few years ago.

Stated briefly, the theory or hypothesis is as follows: There occurs in typhoid fever, in response to the cytogenic stimulus of the typhoid bacillus, a tremendous proliferation of cells in all the lymphoid tissues of the body. Numerically, this pro-

[1] Read May 5, 1909.

[2] Internal Secretions; Metabolic Toxemia. Philadelphia Medical Journal, February 4, 1899.

liferation is as much beyond computation or conception as the pullulation of the bacteria themselves. All cell multiplication is attended by the elaboration of metabolic substances which enter the lymph stream and, by way of it, the general circulation. When the cells die, which in typhoid fever happens soon after their birth, their disintegration products—the analogues of the endotoxins of bacteria—are also poured into the blood. Is it not conceivable that these two groups of substances one produced during cell formation, the other during cell destruction - are a factor in the toxemia and play a part in the causation in the general symptoms of the disease? Granting even that the products of metabolism of the newly formed lymphoid cells and their disintegration products are normal to the body, the quantitative increase occurring in a comparatively short time must tend to swamp the system. But it is more than probable that the metabolic products in the circumstances are abnormal.

That in the formation of the cells and of the bacteria enough proteid or other material is taken from the blood to make a difference is unlikely, although the point is worth considering.

Whatever the source of the poisons, it is eminently desirable to have a method that will eliminate them. Clinicians have endeavored to promote elimination by giving large amounts of water by the mouth and salt solution in considerable quantities by the rectum.

The good results obtained by surgeons in the treatment of peritonitis and other abdominal inflammations and in grave postoperative conditions by the Murphy method of *continuous* enteroclysis led me to use this method in the treatment of typhoid fever. It seemed rational to suppose that the constant instillation of salt solution into the bowel would better accomplish the result aimed at by the administration of water, namely, the filling of the bloodvessels and the increased excretion of poisons. I am aware of the fact that hitherto no positive proof has been brought that soluble poisons, at least none of an albuminous nature, are eliminated in the urine in typhoid fever; however, there is nearly always a pronounced bacilluria.

By the Murphy method it is possible to introduce into the system extraordinary quantities of fluid. Murphy mentions the case of a child, aged eleven years, that absorbed, without losing one drop, thirty pints of salt solution a day. Such quantities I have not succeeded in introducing, nor have I attempted it, but it is easy to secure the absorption of from one-half to one gallon per day.

The method, termed proctoclysis by its inventor, is described as follows:

"The patient is placed in the Fowler position. The apparatus in its simplest form consists of a fountain syringe or can, with a large rubber tube attached, terminating in a vaginal hard rubber or glass tip flexed at an obtuse angle two inches from its tip, having numerous openings in its bulbed end. The tip should be inserted into the rectum so that the angle fits closely to the sphincter, and the tube may then be bound firmly to the thigh with adhesive strips, so that it may not be expelled. The bag or can is suspended from the foot of the bed so that its base is about six inches above the level of the patient's buttocks. Once the irrigating apparatus is thus placed, it need not be disturbed for several days unless to increase or diminish the speed of influx. The solution, consisting of a dram each of sodium chloride and calcium chloride to the pint of water, is now placed in the reservoir and kept at a temperature of 100° F. by applied heat in the form of hot-water bags, thermolytes, or an incasing can of hot water. The quantity administered depends upon the severity of the case, the age of the patient, and other considerations that will suggest themselves in the particular instance.

"The best plan is to place a pint and a half of the saline solution in the container every two hours. The container should be elevated sufficiently to allow this all to flow into the rectum in forty to sixty minutes, giving the rectum a period of rest from the influx of fresh fluid for approximately an hour before it flows again."

I began the treatment by this method, somewhat modified, in the spring of 1908. At first I put the patients in the Fowler

position, but found they did not bear this well. They were then left in bed in the recumbent posture. The solution used was the ordinary normal salt solution, and did not contain calcium chloride. No difficulty was experienced in keeping the tube in place without any special device. The solution flowed in so gently that hardly any was expelled. Occasionally a patient would object to the irrigation, but the majority bore it without a murmur. I have generally discontinued the instillation during the night, and have persisted in it during the day, with brief interruptions in some instances. It would seem that the injection might be given with advantage throughout the febrile stage of the disease, yet it is conceivable that if absorption should not occur promptly the accumulation of water might distend the bowel, a thing not to be desired in the later stages of the disease. Careful observation of many cases will determine whether it is wise to continue the instillation through the third week.

On account of the rarity of typhoid fever in Philadelphia at this time, as a result of the extension of the filtered water system, the opportunity of testing this or any other treatment is inadequate for the drawing of definite conclusions. Large as is the service at the Philadelphia Hospital, I have had since October, 1908, scarcely more than one or two cases of typhoid fever at any one time and the total number is very small. The same condition prevails in the other hospitals.

During the past summer we had a series of ten cases at the Jewish Hospital, several of them of great severity, in all of which the Murphy method of treatment was used; all recovered. The conclusions, however, can only be tentative, and all that we can at present say of the treatment is that it does two things: (1) It increases the flow of urine; (2) it lessens the nervous symptoms. It is difficult to say whether or not it shortens the course of the disease. It has seemed to me, however—and this opinion is shared by my hospital internes—that on account of it we have had recoveries in several desperate cases.

I have presented the subject in this brief way in the hope that those who have an opportunity may give the method a trial.

THE AGGLUTINATION OF HUMAN AND RABBIT BLOOD CORPUSCLES BY CROTALUS VENOM.[1]

By JOSEPH McFARLAND, M.D., and PAUL G. WESTON, M.D.

That venoms produce changes in the blood and affect its corpuscles has long been known, though attempts to demonstrate and interpret the nature of the changes have met with but partial success.

Mitchel and Reichert[1] found that venoms "render the blood incoagulable," and also found that "among the most remarkable effects of venom is that upon the red corpuscles. These bodies undergo substantial modification, *i. e.*, they lose their biconcave shape, become spherical and softened, and fuse together into irregular masses, acting like soft elastic colloid material. This jelly-like condition of the corpuscles is no doubt doubly important in connection with the extravasation of the blood and its probable interference with the normal respiratory function of the blood cells."

Cunningham[2] studied a number of venoms, and concluded that they were primarily blood poisons and caused death by asphyxia, depending upon the loss of oxygen-absorbing power of the corpuscles.

Mitchell and Stewart[3] mixed 20 c.c. each of blood and venom (crotalus?), and observed that "the erythrocytes at once became globular, 3 to 5 microns in diameter, and more highly refractive. The color changed from a greenish-yellow to a light

[1] Read May 5, 1909.

chocolate tinge, and in many of the slides the corpuscles became quite adherent, sticking together in large clumps or drawn out in long stringy masses. These strings of corpuscles often show the erythrocytes drawn out to the length of 20 microns. The tendency of the corpuscles to form rouleaux seemed to have entirely disappeared. The leukocytes were reduced from 18 to 20 microns to 10 to 12 microns in diameter, and became more highly refractive at the borders. The ameboid movement at once entirely disappeared. Examination in twenty-four hours showed the erythrocytes losing color, the strings having disappeared; but the aggregation in clumps was still marked where the layer of corpuscles was very thin. In the very thin layer of blood the formation of small oblong crystals from the erythrocytes was noted. . . . Examination in one hundred and forty-four hours showed the erythrocytes in the majority of the slides to have lost nearly all their hemoglobin. . . . But there was no sign of any general disintegration of the corpuscles."

Stephens and Myers[5] studied the hemolytic action of venom. They found that when cobra venom is added to shed blood in vitro, destruction of the corpuscles (hemolysis) and retardation of coagulation take place. They also found that the hemolytic power of the venom was checked by the antivenomous serum. In a subsequent paper they investigated the relation of cobra venom to the coagulation of the blood.

Myers[6] later studied the hemolytic substance "cobralysin" of the cobra venom and found it destroyed by heat. During these studies he found that the susceptibility of the erythrocytes to cobralysin in vitro bears no relation to the susceptibility of the animal to subcutaneous intoxication by the venom.

Physalix[7] studied the coagulability of the blood under the influence of various venoms, and came to the conclusion that "the conditions that have to do with coagulability of the blood in venom poisoning are numerous and complex and that we are not yet able to explain the phenomena."

Stephens[8] found that the hemolytic constitutuents of snake toxins are not identical.

Myers[9] made further studies of the venom hemolysins and the serum antihemolysins.

Mitchell and Flexner[10] and Flexner and Noguchi[11] have further studied the phenomena of agglutination, hemolysis and leukolysis, and the germicidal properties of the blood serum. They found that the phenomena of agglutination appeared rapidly in favorable solutions, while in weak solutions a delay of some minutes up to one hour might be noted. Active agglutination took place in 0.2 per cent. solutions, while weaker ones either produce no change at all or show imperfect fusion. They studied corpuscles of the dog, rabbit, guinea-pig, sheep, ox, pig, necturus, and frog. The phenomena of hemolysis were found to be complicated. Solutions of 0.2 per cent. were found most favorable for bringing out the hemolytic property, though the different venoms differed considerably, cobra venom being most active, water-moccasin, copperhead, and rattlesnake venoms less so in the order named. They also found that the corpuscles of different animals differed in their susceptibility to the action of the venom, dog's blood being most easily affected, those of the ox least so. The intermediate animals, in order of susceptibility, were sheep, guinea-pig, pig, and rabbit. Solutions of 5 per cent. were needed to hemolyze the corpuscles of the ox. Heating to 75° to 80° C. for thirty minutes does not diminish the hemolytic action of any venom; heating to 90° to 96° C. diminishes the activity of rattlesnake venom; heating to 100° C. for fifteen minutes diminishes the hemolytic activity of cobra, moccasin, and copperhead venom a little.

They believe that venoms contain various intermediate bodies, not all of these being absorbed by any one kind of corpuscles. Venom leukolysis was carefully studied, and they found that venom contained principles that are agglutinating and dissolving for white corpuscles, of which the agglutinating principles may be identical with those for the erythrocytes. The dissolving principle for leukocytes is distinct from that for the erythrocytes. The several varieties of white cells show different susceptibilities to the action of venom.

Flexner and Noguchi[12] found that venoms had a cytolytic

action upon many different cells, probably through a plurality of amboceptors they contain.

Kyes[13] found that hemolysis by venom bore a definite relation to the lecithin content of the blood by which the venom amboceptor was activated.

Noguchi[14] found that the hemolytic principle of venom extended over a wider group of animals than the agglutinating principles, its activity diminishing as the vertebrata were more and more widely departed from. Cobra venom contains the largest, crotalus venom the smallest, number of hemolytic units, while moccasin venom contains the greatest number of agglutinating units for such blood. The mechanism of hemolysis is identical with that for the blood of warm-blooded animals. Complements are, therefore, present in all vertebrates and many, at least, invertebrate species. The heat liability of the venom agglutinins and hemolysins for cold-blooded animals agrees closely with that for warm blooded animals.

Lamb[15] studied the phenomena of hemolysis resulting from the venoms of Indian and Australian snakes and crotalus adamanteus.

This survey of the work accomplished shows that the effects of venom upon the blood may be divided into those affecting coagulation, those agglutinating the erythrocytes, those agglutinating the leukocytes, those dissolving the erythrocytes, those dissolving the leukocytes, and those effecting the destruction of bacteria by the serum.

The studies that we wish to report in this paper have to do with the phenomena of agglutination and deal particularly with the agglutinative phenomena of crotalus venom upon human blood corpuscles, a subject that does not seem to have been studied before.

The technique used was as follows: The finger was punctured and from 2 to 5 c.c. of blood collected in a small sterile tube and immediately defibrinated. The tube was then placed in the centrifuge, the corpuscles sedimented and the clear serum removed with a pipette. An equal quantity of 0.85 per cent. sodium chloride solution was next added, the corpuscles thoroughly mixed with it

by active shaking, and the tube returned to the centrifuge. In this way the corpuscles were washed three times, and finally suspended in twenty times their volume of the saline solution.

The venom used was in the dry state, but a fresh solution was prepared each day that tests were made.

In making the tests, 1 c.c. of the corpuscle suspension was added to each of a series of sterile test-tubes. Varying quantities of the venom solution were then added and the mixture thoroughly shaken. Each tube then received 0.5 c.c. of a threefold dilution of normal human serum (serum 1, saline solution 2) and the contents of each tube brought up to exactly 2 c.c. by the addition of sterile saline solution. The mixture was well shaken, placed for one hour in the thermostat at 37.5° C., and then kept over night in the ice box. The next day the tubes were removed, shaken, and centrifugalized for five minutes. Since hemolysis was studied at the same time as agglutination, serum was added to each tube. Control tubes were always prepared with each series of experiments. The time expressed in the following tabulations refers to the appearance of masses visible to the unaided eye.

To assist in constructing the tables we make use of the following signs:

A, means that the agglutinated corpuscles formed a flocculent precipitate; AA, that large masses of agglutinated corpuscles were found; AAA, that the corpuscles formed a clot-like mass at the bottom of the tube, leaving the supernatant liquid clear.

As hemolysis more or less marked usually accompanied or succeeded the agglutination, we employ the following signs to express it: H, means that there was a trace of red color in the fluid; HH, that the fluid was quite red; HHH, that the fluid was very red, and the sediment of corpuscular stroma practically colorless; HC, that the corpuscles were both hemolyzed and their stroma dissolved.

EXPERIMENT I.

Tubes.	Grams of dry venom of crotalus adamanteus in the total quantity of the final mixture.	5 per cent. suspension of human erythrocytes in 0.85 per cent sodium chloride solution.	Normal human serum diluted with two volumes of sodium chloride solution.	Results.
	0.0000125	0.1 c.c.	0.5 c.c.	O + O
	0.000125	"	"	O + H
1	0.001	"	"	A + H 30 minutes
2	0.01	"	"	AA + H
3	0.05	"	"	AA + HHH
4	0.06	"	"	AAA + HHH 3 to 5 minutes
5	0.1	"	"	AA + HH 3 to 5 minutes
6	0.2	"	"	AAA + H immediate

Note that there is no constant relation between agglutination and hemolysis. In tubes 1, 2, and 3 agglutination and hemolysis progressed uniformly, but in 4, 5, and 6, though the degree of agglutination was the same and its rapidity increased, hemolysis diminished.

That the addition of more serum causes agglutination to take place slowly but does not affect the amount is shown by Experiment II.

EXPERIMENT II.

Tubes.	Grams of dry venom of crotalus adamanteus in the total quantity of the final mixture.	5 per cent. suspension of human blood corpuscles in 0.85 per cent. sodium chloride solution.	Normal human serum diluted with two volumes of sodium chloride solution	Results.
1	0.1	1 c.c.	1 c.c.	AAA slow
2	0.4	"	"	AAA + H slow

This shows that the addition of an excess of serum results in retardation of agglutination and inhibition of hemolysis.

It was now noted that when the dry venom was dissolved in the salt solution preliminary to making the experiments, there was always a certain amount of mucoid substance in the solution.

It was also discovered that the venom was not sterile. It was therefore decided to refine and sterilize the venom by the following means:

Five grams of the crotalus venom was dissolved in just as little salt solution as possible, and filtered through a hardened filter paper. The perfectly clear filtrate was evaporated to dryness, finely powdered, placed in a sterile tube, covered with chloroform and plugged with cotton. The tube was then placed in the thermostat until the chloroform evaporated, which took a couple of days.

Venom so prepared was sterile, but it had been exposed to chloroform, and it contained a slight increase of sodium chloride. It therefore became necessary to determine whether its agglutinating and hemolyzing properties had changed. To this end Experiment I was repeated with a slight modification in the venom quantities employed (see Experiment III).

EXPERIMENT III.

Tubes.	Grams of dry venom of crotalus adamanteus in the total quantity of the final mixture.	5 per cent. suspension of human erythrocytes in 0.85 per cent. sodium chloride solution.	Normal human serum diluted with two volumes of sodium chloride solution.	Results.
1	0.04	1 c.c.	0.5 c.c.	AA + HH
2	0.052	"	"	AA + HHH
3	0.06	"	"	AAA + HHH
4	0.1	"	"	AAA + HHH
5	0.15	"	"	AAA + HHH
6	0.2	"	"	AAA + H

Comparison with Experiment I will show that the exposure of the venom to chloroform does not affect either the agglutinating or the hemolytic properties.

The quantity of venom to be dissolved in the mixture was found to be greater than could easily be taken up, so that it became necessary to change from a total of 2 c.c. to 10 c.c. As this altered the concentration of the mixture, it was necessary to

determine whether the alteration affected the agglutinative and other phenomena. To this end a series of experiments was done, the results of which are shown in Experiment IV. No change was found to follow dilution of the mixture without change in the proportions of ingredients.

EXPERIMENT IV.

Tubes.	Grams of dry venom of *Crotalus adamanteus* in total quantity of final mixture.	5 per cent. suspension of human erythrocytes in 0.85 per cent. sodium chloride.	Normal human serum diluted with two volumes of sodium chloride solution.	Results.
1	0.01	1 c.c.	0.5 c.c.	AA+H
2	0.03	"	"	AA+HH
3	0.05	"	"	AA+HHH
4	0.07	"	"	AAA+HHH

Comparison with the results shown in Experiment I shows that simple dilution without alteration of the proportions of the ingredients did not affect the results.

It was thought that the technique might be simplified by the employment of citrated blood instead of defibrinated blood, but as the corpuscles in defibrinated blood may lose something in the formation of the fibrin, and as the citration may effect some independent change in the corpuscles, the new technique had to be tried and the results compared with those already obtained.

Accordingly, blood from the finger tip was permitted to drop into a tube containing a 2 per cent. solution of sodium citrate in 0.85 per cent. sodium chloride. As soon as sufficient was obtained the tube was placed in the centrifuge and the corpuscles collected and washed as usual. Of these washed corpuscles a 5 per cent. suspension was prepared and a series of tests made, the results of which are shown in Experiment V. A glance at the table shows that there was no difference in the end reaction in regard to agglutination or hemolysis, though the reaction was delayed when corpuscles from citrated blood were employed.

EXPERIMENT V.

Tubes.	Grams of dry venom of crotalus adamanteus in total quantity of the final mixture.	5 per cent. suspension of human erythrocytes in 0.85 per cent. sodium chloride solution.	Normal human serum diluted with two volumes of sodium chloride solution.	Results.	
				Defibrinated blood.	Citrated blood.
1	0.01	1 c.c.	0.5 c.c.	AAA+H 10 to 15 min.	AAA+H 20 to 30 min.
2	0.03	"	"	AAA+HH 5 to 8 min.	AAA+H 8 to 10 min.
3	0.05	"	"	AAA+HH 3 to 5 min.	AAA+HH 5 to 8 min.
4	0.07	"	"	AAA+HHH 1 to 3 min.	AAA+HHH 3 to 5 min.

From this experiment it appears that citration of the blood nearly doubles the time of agglutination and hemolysis as compared with defibrination, though the end results are the same.

It became interesting to learn whether the citrated plasma could be employed in lieu of the serum from the defibrinated blood, seeing that it contained not only the citrate of sodium, but also the fibrinogenic elements.

To this end Experiment VI was performed, which shows again that though the end reactions were the same, the reaction took place much more rapidly in half the time when the serum from the defibrinated blood was employed.

EXPERIMENT VI.

Tubes.	Grams of dry venom of crotalus adamanteus in total quantity of final mixture.	5 per cent. suspension of human erythrocytes in 0.85 per cent. sodium chloride solution.	Normal human serum from defibrinated blood diluted with two volumes of sodium chlorate solution.	Results.
1	0.06	1 c.c.	0.5 c.c.	AAA 18 min.
2	0.06	"	"	AAA 8 min.
			Normal human plasma from citrated blood diluted with two volumes of sodium chloride solution.	
3	0.06	1 c.c.	0.5 c.c.	AAA 20 min.
4	0.06	"	"	AAA 15 min.

Comparison of these results shows that the time of agglutination was retarded by the use of citrated plasma, though the end reaction was the same as with the serum obtained by defibrinating the blood.

It was found possible to measure the agglutinating substance by making it combine with corpuscles until it became exhausted. Thus, Experiment VII shows that 0.125 gram of venom contains an amount of agglutinating substance exhausted by absorption by 0.35 c.c. by volume of corpuscles thrown down by the centrifuge. When the same experiment was tried with rabbit's corpuscles it was found that they possessed a far greater affinity for the agglutinogenic substance than human corpuscles do, 1 c.c. of human corpuscles exhausting the agglutinin in 0.357 gram of venom, while 1 c.c. of rabbit corpuscles takes up the agglutinin in 0.8333 gram of venom (compare Experiment VII, A and B).

EXPERIMENT VII.—A. *Human Corpuscles.*

Grams of dry venom of crotalus adamanteus in total quantity of final mixture.	5 per cent. suspension of human erythrocytes in 0.85 per cent. sodium chloride solution.	Normal human serum diluted with two volumes of sodium chloride solution.	Results.
0.125	1 c.c.	0.5 c.c.	AAA
The mixture	was then centrifugalized and to it more corpuscles added		
	1 c.c.	.....	AAA
The mixture	was then centrifugalized and to it more corpuscles added		
	1 c.c.	.....	AAA
The mixture	was then centrifugalized and to it more corpuscles added		
	1 c.c.	.....	AAA
The mixture	was then centrifugalized and to it more corpuscles added		
	1 c.c.	.....	AAA
The mixture	was then centrifugalized and to it more corpuscles added		
	1 c.c.	.....	AA
The mixture	was then centrifugalized and to it more corpuscles added		
	1 c.c.	.....	A
			Microscopic agglutinations were to be found

EXPERIMENT VII.—B. *Rabbit Corpuscles.*

Grams of dry venom of crotalus adamanteus in total quantity of final mixture.	5 per cent. suspension of human erythrocytes in 0.85 per cent. sodium chloride solution.	Normal human serum diluted with two volumes of sodium chloride solution.	Results.
0.0125	1 c.c.	0.5 c.c.	AAA
This mixture	was centrifugalized	and to the fluid mo re corpuscles added	
	1 c.c.	.....	AAA
This mixture	was centrifugalized	and to the fluid mo re corpuscles added	
	1 c.c.	.....	A
			Few small agglutinated masses were found

Our next experiment was performed for the purpose of determining whether the agglutination of human corpuscles corresponded with that of other blood, and, as most easily obtained, rabbit's blood was first employed. The blood was secured from the carotid artery of the rabbit by means of a cannulated tube, and the experiment was made to include parallel series of tubes in which the agglutination of corpuscles from defibrinated blood acted upon by venom and citrated plasma might be compared with corpuscles from defibrinated blood acted upon by venom and serum. Experiment VIII shows that rabbit's blood behaved in this regard exactly like human blood in that the agglutination of the corpuscles takes place more slowly when citrate is used, though the end reaction is the same.

EXPERIMENT VIII.—A.

Tubes.	Grams of dry venom of crotalus adamanteus in total quantity of final mixture.	5 per cent. suspension of rabbit corpuscles from citrated blood in 0.85 per cent. sodium chloride solution.	Normal citrated rabbit's plasma diluted with two volumes of sodium chloride solution.	Results.
1	0.0000125	1 c.c.	0.5 c.c.	0
2	0.000125	"	"	A
3	0.00125	"	"	AA
4	0.0125	"	"	AAA
5	0.125	"	"	AAA

EXPERIMENT VIII.—B.

Tubes.	Grams of dry venom of crotalus adamanteus in total quantity of final mixture.	5 per cent. suspension of rabbit corpuscles from defibrinated blood in 0.85 per cent. sodium chloride solution.	Normal rabbit's serum diluted with two volumes of sodium chloride solution.	Results.
1	0.0000125	1 c.c.	0.5 c.c.	O
2	0.000125	"	"	A
3	0.00125	"	"	AA
4	0.0125	"	"	AAA 5 min.
5	0.125	"	"	AAA 5 min.

From this experiment it will also be observed that 0.000125 gram is sufficient to produce the first appearance of agglutination of rabbit's corpuscles, as contrasted with 0.001 gram, the smallest quantity that will produce agglutination of human corpuscles, thus showing that the rabbit corpuscles are more susceptible to the action of the venom (compare Experiment I).

It has been found by Flexner and Noguchi that heating venom for thirty minutes at 75° to 80° C. destroys the agglutinins but does not affect the hemolysins. They do not say whether it is the dry venom or the solution that is heated, but we concluded that it was the latter that was meant. We therefore repeated their work according to the technique used by us, and found the statement correct both with regard to human erythrocytes and rabbit erythrocytes. The results are shown in Experiment IX.

EXPERIMENT IX.—A. *Heated Venom Solution.*

Tubes.	Grams of dry venom of crotalus adamanteus in total quantity of final mixture. The solution of venom had been heated over a water bath for thirty minutes at 75° to 80° C.	5 per cent. suspension of human erythrocytes suspended in 0.85 per cent. sodium chloride solution.	Normal human serum diluted with two volumes of sodium chloride solution.	Results.
1	0.0002	1 c.c.	0.5 c.c.	O
2	0.0005	"	"	O
3	0.0007	"	"	O
4	0.001	"	"	O
5	0.0015	"	"	O
6	0.07	"	"	O

EXPERIMENT IX.—B.

Tubes.	Grams of dry venom of crotalus adamanteus in total quantity of final mixture. The solution of venom had been heated over a water bath for thirty minutes at 75° to 80° C.	5 per cent. suspension of normal rabbit erythrocytes in 0.85 per cent. sodium chloride solution.	Normal human serum diluted with two volumes of sodium chloride solution.	Results.
1	0.0002	1 c.c.	0.5 c.c.	O
2	0.0005	"	"	O
3	0.0007	"	"	O
4	0.001	"	"	O
5	0.0015	"	"	O
6	0.07	"	"	O

We were curious to know whether the same destructive action upon the agglutinins would follow similar heating of the dry venom. Accordingly, some was finely pulverized, spread over the bottom of a small flask, and floated upon the surface of a water bath, the temperature being kept for thirty minutes at 75° to 80° C. The heated venom was then dissolved as usual, and the experiment made. It is interesting to note that when the saline solution was added to this heated, powdered venom, solution was immediate. It was found that although the solubility of the venom was thus affected, its agglutinative activity upon the erythrocytes was scarcely changed, as is shown by reference to Experiment X. When the venom was heated for one hour in the dry state, the results were the same. This shows that whatever the agglutinin is, it is scarcely at all affected when dry, though easily destroyed by the same degree of heat when in solution.

EXPERIMENT X.—A. *Effect of Heating Dry Venom.*

Tubes.	Grams of dry venom of crotalus adamanteus in total quantity of final mixture. The venom was powdered and heated thirty minutes to 75° to 80° C. in the dry state.	5 per cent. suspension of normal human corpuscles in 0.85 per cent. sodium chloride solution.	Normal human serum diluted with two volumes of sodium chloride solution.	Results.
1	0.002	1 c.c.	0.5 c.c.	O
2	0.03	"	"	AA
3	0.05	"	"	AA
4	0.07	"	"	AAA

Experiment X.—B.

Tubes.	Grams of dry venom of crotalus adamanteus in total quantity of final mixture. The venom was powdered and heated thirty minutes to 75° to 80° C. in the dry state.	5 per cent. suspension of normal rabbit corpuscles in 0.85 per cent. sodium chloride solution.	Normal human serum diluted with two volumes of sodium chloride solution.	Results.
1	0.002	1 c.c.	0.5 c.c.	AA
2	0.03	"	"	AA
3	0.05	"	"	AAA
4	0.07	"	"	AAA

Conclusions.

1. The rapidity of agglutination of human corpuscles by crotalus venom increases with increase of the quantity of venom employed.

2. The agglutination of the corpuscles takes place independently of hemolysis.

3. Chloroform has no effect upon the agglutinating or hemolyzing effects when added to dry venom for the purpose of sterilizing it.

4. Corpuscles from citrated blood are agglutinated more slowly than those from defibrinated blood.

5. Corpuscles agglutinate more rapidly when serum is present, though an excess of serum retards agglutination.

6. Rabbit's corpuscles have a greater agglutinin absorbing capacity than human corpuscles.

7. Rabbit's corpuscles are more sensitive to venom agglutinin than human corpuscles.

8. The agglutinins are destroyed when the venom solutions are heated to 75° to 80° C. for thirty minutes.

9. The agglutinins are scarcely at all affected when the dry powdered venom is heated to 75° to 80° C. for an hour.

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DISCUSSION.

Dr. Paul G. Weston: I should like to say that in the experiments where five-tenths cubic centimeter of serum dilution were used, the results were constant for agglutinins. It will be noticed that increasing doses of venom caused increased agglutination in each experiment, but after a certain point was reached hemolysis began to diminish. We then tried adding one cubic centimeter of the serum dilution instead of five-tenths, and found that agglutination was much less, and the same applies to hemolysis. With citrated plasma the end results were the same, but the time required for the reactions was increased.

EPILEPSIA PARTIALIS CONTINUA OCCURRING IN CEREBRAL SYPHILIS.[1]

REPORT OF A CASE, WITH OPERATION.[2]

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It seems almost incredible that any form of epilepsy should exist and yet not be well recognized. The literature of this disease is very extensive, and much of it contains little that is new. There is a type of epilepsy, however, which does not appear in the text-books, and even in the most recent writings receives scant recognition. Thus, Oppenheim[3] mentions it in a few lines by stating that cases occur in which during the interparoxysmal period muscular twitchings of short duration and without loss of consciousness are observed in one or another portion of the body. It has been described, especially by Russian writers, as "epilepsia continua" (Koshewnikow, Muratoff, Bechterew); Bruns also mentions it.

The cases differ from those of myoclonic epilepsy; the twitchings are limited to a small portion of the body, and are more intense than in myoclonia.

The name "epilepsia partialis continua" seems to have been first employed by Koshewnikow,[4] who reported four cases in 1894.

[1] Read June 2, 1909.

[2] From the Philadelphia General Hospital and from the Laboratory of Neuropathology of the University of Pennsylvania.

[3] Lehrbuch der Nervenkrankheiten, ed. 5, p. 1389.

[4] Neurol. Centralbl., 1895, p. 47.

Characteristic epileptic attacks occurred in all four cases; sometimes they were abortive, sometimes they were with loss of consciousness. No period of cessation occurred between these attacks, as in certain portions of the body clonic movements persisted with variation in intensity, and when these movements became very severe they passed into an ordinary epileptic convulsion. The patients were unable to work, as they held the twitching limbs with those not implicated by the movements. In two of the cases the disorder began with local spasm, which passed into the ordinary epileptic convulsion; in the other two the persistent clonic movement followed the ordinary epileptic attack. No information as regards pathology was obtained either by operation or necropsy. This form of epilepsy has, since the report of these cases, been called, by some writers, Koshewnikow's epilepsy.

Orlowski[1] reported a case of this type in which general epileptic attacks occurred after an infectious disease, and later the patient had attacks every ten or fifteen minutes without loss of consciousness. Twitching of fibrillary or tic-like character was seen in the right side of the face, implicating also the tongue and larynx and continuing during sleep. The right limbs were weak. The case was thought by some of those who heard the report to be functional and not organic. No pathological cause was determined.

Choroschko has written a monograph on this form of epilepsy, but, as it is in the Russian language, I have been obliged to depend on abstracts.[2] In the *Jahresbericht für Neurologie und Psychiatrie*, 1907, it is stated that Choroschko reports three cases of his own and refers to eleven in the Russian literature. Outside of Russia, Bruns alone has observed this rare type. Choroschko differs from Koshewnikow in that he believes the lesion is subcortical and suggests the name "polyclonia epileptoides continua." The twitchings are clonic and extend gradually from a limited area, and usually synergetic muscles are affected, especially on the right side. There seem to have been no lesions found either by operation or necropsy, so far as one may judge from the abstracts.

[1] Neurol. Centralbl., 1896, p. 526.

[2] Choroschko. Neurol. Central., 1908, p. 279; Jahresb. f. Neurol. u. Psychiat., 1907, p. 772.

It may not be amiss, therefore, to report a typical case of this partial constant epilepsy, especially as it is one in which operation was performed. It shows that the lesion may be cortical.

History. The patient, a colored man, aged twenty-two years, was admitted to my service at the Philadelphia General Hospital, February 19, 1908. He gave a clear history of syphilitic infection. In July, 1908, he had his first convulsion. The fingers of the right hand twitched at first slightly, but later more severely, and the convulsion confined to these members lasted about twenty minutes and left a paralysis of the hand persisting about fifteen minutes. He had another convulsive attack confined to the right hand in about three weeks. The whole right upper limb became implicated in the third attack, and this attack was followed by unconsciousness. There seems to have been involvement of the face and right lower limb also in the fourth attack. After these repeated attacks persistent weakness of the right upper limb ensued.

Examination. The weakness of the right side of the face increased greatly after the man entered the hospital, and the palsy was of the cerebral type, *i. e.*, slight in the upper part of the face and almost complete in the lower part. The weakness of the right upper limb also increased considerably, and the right biceps and triceps reflexes were much exaggerated, whereas the corresponding reflexes on the left side were normal. Stereognostic perception and sense of position were lost in the right hand. Tactile sensation also seemed to be diminished in this part, but was normal in the face. The motor power was about normal in the lower limbs, and the patellar reflex was only a little prompter on the right side. Babinski's sign was not distinct on either side. The ocular examination revealed little that was abnormal.

The case was clearly one of syphilis of the brain with convulsions of the Jacksonian type, only the right side of the body being involved, and the persistent paralysis being confined to the right side of the face and the right upper limb. Other attacks which the patient had made the case an unusual one and worthy of careful study.

Independently of the typical attacks, he had twitching confined to the right side of the face lasting an indefinite period, an hour or more at a time and occurring very frequently. There were periods in which he had none of these spasmodic movements, but the movements were almost constantly present, and resembled a tic movement or fibrillary twitching. They were not excessive in their intensity, and implicated the muscles about the right side of the mouth, about the right eye, the right cheek, the right ear, and the right side of the neck. After persisting for some weeks in the face they ceased in this part, and were observed in the right upper limb. The whole right upper limb was displaced in these clonic movements, but the displacement was not excessive, and the

spasm consisted of slight twitchings lasting indefinitely as did the previous twitchings of the right side of the face. There was no impairment of consciousness. The peculiarity was the almost constant duration of fibrillary or twitching movements in the face at first and later in the right upper limb, movements that were very unlike the severe spasmodic contractions usually seen in an epileptic attack, both in intensity and duration.

It is a question whether operation is advisable in cerebral syphilis. Two cases with operation have been observed by me in addition to the one described in this paper; in one the removal of a gumma of the dura was followed by much improvement during a period of seven or eight years, but the patient eventually died of his syphilis. In another case excision of a gumma of the brain was performed, but the result was far from satisfactory, and in the case reported in this paper operation accomplished little. However, as there seemed to be a chance for the patient from operation, I referred him to Dr. Edward Martin, whose report is here given.

Because of the failure of mercury and iodide treatment, the steady progression of symptoms, the possibility of their leading to a fatal termination, operation was deemed advisable in this case. The Rolandic area was exposed by a periosteal flap which was raised by means of a Crile cutting tool driven by an electric engine. The dura was raised without difficulty, exhibiting only slight adhesion to gummata placed in the arm and face centres. A portion of this tissue was excised by circular excision, the obvious vessels leading to it being first encircled by fine gut carried by means of a fine pointed, curved needle. The operation was attended with trifling shock.

FOUR GENERATIONS OF AMERICAN GOUT.[1]

By ROBERT N. WILLSON, M.D.

THE following series of four instances of chronic food-poisoning in four successive generations is submitted for its diagnostic interest, as well because of its value in suggesting for therapeutic and hygienic attention the ground condition underlying similar obscure cases.

CASE I was that of a lady in advanced years, who first came under my medical observation in 1901, when in her eighty-eighth year. She had always been a full eater, but did not consider herself unusual in the matter of appetite. The joints of the fingers and toes showed unmistakable gouty changes, and the history given was that of an increasing disability of these small joints. On October 10, 1901, while stepping from a carriage, she felt a severe pain in the right knee, which gave way, letting her down upon the ground. She was in great pain; the knee when seen by me was hot and considerably swollen, and there was some fluctuation evident above and outside the patella. No other joints were involved. On October 12, 1901, both knees and ankles were hot, swollen, and tender. This condition gradually subsided under practical starvation and overfree evacuation of the bowels, and within a few days entirely disappeared. The temperature was never above 99° F.; the heart showed no sign of involvement; the urine was high colored, full of urates, and contained a faint trace of albumin.

From that time until the death of the patient, one year ago, at the age of ninety-three, there were recurrent mild attacks of a similar nature, invariably controlled by and through the dietary, and by artificial evacuation and cleansing of the intestinal tract. Very frequent had been the occurrence of urticaria, sometimes synchronously with the joint involvement, oftentimes alone. A vegetable, restricted diet enabled the patient to remain entirely free from symptoms, but was so seldom tolerated by her that the discomfort consequent upon

[1] Read June 2, 1909.

an oversupply of food was for the most part present. This varied according to the gravity of the offence (measured in terms of food quantity) and its duration, far more distinctly than with the variation in the kind of food.

Case II was that of an otherwise healthy man, aged sixty-one years, of sedentary habits, an excessive smoker, and an admittedly rapid eater. His food supply, while always generous, never amounted to an apparent excess for the average man. He first came under my care in 1900, shortly before I saw and studied the case of his mother, just described. In 1892 he had been in bed for several months with sciatica, following an accidental blow on the head. Since that time more markedly than before he had noticed a fulness of the abdomen, dizziness, belching, fugitive pains in the head, general discomfort, and a sense of heat throughout the body. The occiput and nape of the neck felt heavy, and sometimes even ached. There was considerable flatus, and discomfort in the abdomen. The mouth tasted bad, lights were seen dancing before the eyes, and there was some palpitation.

The urine was high colored and full of uric acid and sodium urate crystals.

Since first studied by me there have been many disappearances and just as many recurrences of this picture. Occasionally patches of eczema would appear over the dorsal surface of the hands, or on the arms. Once a large area (the size of the palm of the hand) appeared swollen, red, and tender, in the left hypochondrium, and subsided without notice, as though an angioneurotic edema. There has been considerable stiffness and heaviness in the right leg, particularly from the knee down. This he attributes to the accident and to the blow upon the head already noted. Occasionally the movements of the ankle and foot "have not been easy or natural." "This has always passed away." There has occasionally been an aching of the shin bone and the calf of the leg, and a numbness of the toes. All of the symptoms have recently diminished and many have disappeared.

In May, 1905, during a series of symptoms similar to those just narrated there appeared a crop of suppurating blebs between the toes of both feet, also a few upon the under surface of the toes, and in the cracks and crevices of the under surface of the feet. First seeming abrasions, then blebs, then pustules made their appearance. Lymphangitis of the right leg followed the red lines running to the groin. The patient's condition was a distinctly septic one for two days, and then settled to the normal. On milk diet and in bed the feet healed, and in a week's time appeared well. Immediately upon the resumption of solid food the blebs and pustules would recur, to subside again with its withdrawal. There was an excess of acid, offensive perspiration between the toes, and the tissues seemed to break down under its influence unless kept constantly clean. On diet, rest, complete withdrawal of the tobacco, and free evacuation of the bowels, this condition retired, and final convalescence was secured, though only after a siege of three months' duration. The urine during

this period showed the same concentration and, as on each previous occasion, also the overloading with uric acid and its derivatives.

In April, 1909, there was a beginning of a similar involvement of the toes and feet. With the previous experience to guide the line of treatment, however, the duration of the condition was brief, and at the end of a fortnight the skin surface appeared and remained normal.

The indefinite discomfort and the local symptoms upon the skin of the body have occasionally recurred, but, like their congeners of the toes and feet, all have yielded to starvation (tobacco and food) and to asepsis of the intestinal tract.

Case III has been my own, and of especial personal interest, in the light of the two preceding pictures in my immediate ancestors. During boyhood I was able to eat inordinately, and no doubt, as most boys do, so I did. There is little doubt, moreover, that, boy-like, the method of eating was hurried and the mastication imperfect. Nothing untoward transpired in a health record singularly free from a need for medical attention until the year 1902, when, while in the midst of a tennis match, I found myself unable to run because of a sharp pain in my right hip-joint. The next day this pain had nearly disappeared, and to such an extent that I was able to play through the tournament. Frequently through that summer the pain recurred, always suddenly, usually during active exertion, and, as a rule, continuing for the greater part of a day. Usually it was in the hip; sometimes in the right knee. Rarely the right ankle felt heavy and painful. There was never swelling, and the joints were neither red nor hot. I next noticed that in the morning the hands felt puffy and swollen, the eyes tired, and throat and pharynx stiff and even painful. The urine was normal and at no time then or since has contained either uric acid crystals, urates (solid), or albumin. Finally, one night, after severe exercise, I noticed that, although before dinner perfectly free from pain, I rose from the table stiff in the right knee and ankle. For the first time I associated the joint pains with the ingestion of considerable quantities of food, especially after severe exercise, and began to experiment accordingly. I found that up to a certain limit I could eat any and every kind of food. As soon as that limit in quantity had been passed the old joint symptoms, plus those of the face, hands, eyes, and throat, would all make their appearance, and remain for a time corresponding to the excess of food. I found that starvation would relieve the distress, and that purgation would do away with it almost at once. There seemed to be little doubt either as to the etiology, pathology, or treatment indicated. A dietary régime was instituted that absolutely removed the difficulty and for a time prevented its return. Two years ago there occurred another series of symptoms which proved equally perplexing, and was stupidly enough attributed to an entirely mistaken cause. I had been in the habit of using the first joint of my left forefinger as a plessimeter under a metal plessor,

in order to employ to advantage both the sense of hearing and the perception of resistance to the stroke. On the morning following a banquet I noticed a crop of tiny blebs surrounding this joint, and a sense of heat (not pain) in the skin and overlying tissues. My pharynx was stiff and sore, my eyes were watering, I suffered from a profuse coryza, I sneezed incessantly, and, what seemed exceedingly strange at the time, my hands and feet were too large for gloves and shoes. The urine was absolutely normal. In a day every symptom had disappeared; even the joint of the forefinger had become normal. More than once after this the blebs and slight swelling of this joint reappeared, sometimes with, sometimes without, the attendant train of supposedly influenzal symptoms. Invariably the occurrence followed a dietary indulgence between meals, and finally the association became too striking to ignore. I again began to experiment, as frequently as I could persuade myself to endure the discomfort of an old-fashioned influenzal attack. As certainly as I exceeded my heretofore perfectly safe limit, just so inevitably did I pay the penalty. A whole day would go by. Then a general feeling of muscular soreness and exhaustion would appear. The feet and hands would begin to feel swollen; and within twenty-four hours, or much sooner if the excess of food was large, the skin of the first phalanx of the original forefinger would parch and dry up, and later the digital phalanges of the first and second fingers of the left hand also. The dried skin would break out in blebs, with an intense itching that subsided only with a bowel movement, or with distance from the last ingestion of food. The pharynx would become red and granular, it was painful to swallow, mucopus formed in the nasopharynx, and very frequently the voice would become husky to an extent that was as embarassing as ridiculous, the cause being known. My nose would run and the tears flow as though I was suffering from an acute cold. On more than one occasion the irritation of the conjunctiva simulated one caused by a foreign body. The secretion varied from a clear serum to a true laudable pus. Almost invariably the ears felt full and uncomfortable. On one or two occasions there was a scaling and cracking of the skin between the toes. All of these symptoms, especially those experienced locally in the feet and hands, seemed to be exaggerated by any severe nervous excitement. Even when the blebs and swelling in the superficial tissues of the phalanges were subsiding the nervous stimulus of a public discussion or speech, or of the presentation of a scientific paper, or even the stress and hurry of a crowded day's program, would tend to relight their activity, or at least to delay their disappearance. Following a free evacuation of the bowels there was almost immediate partial relief. Sprays, local applications, and the internal administration of drugs made matters only worse. Fortunately the conditions were such as to naturally discourage eating, because the appetite never waned. Finally, it became apparent that the quantity of food ingested in the twenty-four hours, and that alone, was at fault. From that moment the task became simple, though as difficult as it was plain.

If too much was being eaten, less would and must suffice, even if it implied, as it does, a military diet. It appeared that there had developed a tendency to either the need of a diminishing amount of food in spite of a persistent appetite, or a more and more evident contraction in my ability to assimilate food products. That the latter is not the correct explanation of the symptom complex, which I can produce at will and as readily prevent, seems apparent from the perfect maintenance of health and vigor and bodily weight on an amount of food sufficiently low to prevent discomfort and subjective symptoms. That a diminished need plus a family idiosyncrasy best explains the phenomenon became laughably and painfully clear when the tendency reasserted itself in my child.

Case IV has been studied in my little girl, aged four (now five) years, a high-strung child, always under nervous tension, who during the past twelve months has had repeated attacks of a type that her mother has labelled "cold," "la grippe," and everything else besides the proper diagnosis, which only within the very recent past has she been willing to admit into consideration. Always overfed, like every other American child of Anglo-Saxon parentage, this little girl has out of a clear sky repeatedly become hoarse, has coughed day and night, has sneezed when not coughing, and run from eyes and nose until the handkerchief supply has found an end. Relief has been obtained when, and only when, the intestinal tract has been emptied from one end to the other and food altogether withdrawn. Skepticism became so intolerant that I finally challenged the mother to the experiment of deliberately overfeeding the child. She thereby produced a full-fledged, old-fashioned cold that would ordinarily require a week's sojourn in bed. Castor oil and starvation, with the child at rest in bed, furnished a speedy cure. I have so often watched the process of overfeeding in this case result in the gradual production of the now (to me) classical symptoms, that I can nearly calculate their time of appearance by the amount of food administered.

That this case is not sui generis finds ready witness. Only today there was sent to me from Virginia a little girl, aged twelve years, with a history of a long-standing cold, catarrh of the nasopharynx, and constant sneezing. I found her chest and abdomen normal, the lungs and heart absolutely sound. The tonsils were large, and from the nasopharynx dropped steadily a yellowish mucopus. The mother stated that the child had a poor appetite, but on inquiry from the child I learned that the dietary of the day before had been as follows: Food actually eaten: breakfast—one orange, a plate of cereal, beefsteak, three griddle cakes and syrup, a glass of milk, and one slice of bread and butter; dinner—two helpings of meat, two helpings of potatoes and of one other vegetable, bread and butter, pickle, radishes, and dessert; supper—meat, vegetables, and fruit. While in my office this child sneezed five times. Her nasal and pharyngeal mucous membranes were slightly reddened, but otherwise

normal. While the case has not been studied to its end, there is little doubt in my mind that this Southern descendant of our English ancestors is suffering from an inherited overappetite and from the need of a lessened food supply.

The danger from such knowledge as is gained through a superficial study of the above series of cases is apparent. It will furnish a strong temptation to the practitioner to term every cold gout, every influenza food-poisoning, every ache and pain lithemia, every joint swelling an excess of food. On the other hand, carelessness of the significance of signs and symptoms leads to disaster. A few days ago I saw in consultation a trained nurse with a tuberculous apex. Tubercle bacilli have since been found in her feces, and a positive tuberculin reaction has been obtained. There was neither a cough nor a particle of sputum to suggest a pulmonary involvement. The case was sent to me as one with a cardiac lesion.

I publish these records, my own among the number, for what they are worth in interest and value as bits of home study and observation, and as pointers to the need of a discriminating care in diagnosis. Not without practical interest is the evident association in at least two of these cases of two distinct influences, the toxic and nervous, in the production and accentuation of symptoms. If no other lesson were taught and learned, it would be of advantage for us to understand that not every chronic cough and expectoration can be safely regarded as tuberculous in origin; that a moderate amount of food may be an undersupply or an excess for the given individual; and that many a laryngitis and partial aphonia may be rationally attributed to the diet, and cured by a hygienic régime.

A STUDY OF THE METABOLISM OF MYASTHENIA GRAVIS, WITH A SUGGESTION REGARDING TREATMENT.[1]

By RALPH PEMBERTON, M.D.,

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THROUGH the kindness of Dr. W. G. Spiller, an opportunity has presented for the study of the metabolism in a case of myasthenia gravis.

The subject of myasthenia has received attention, in great degree, from neurologists alone, and though the clinical aspects of the disease have been known for a long time, little has been adduced to date regarding the etiology or pathology. It would seem, in view of these facts, that, except for the great rarity of the disease, attempts would have been made to approach it through other channels; but reference to the literature shows that, with few exceptions, this has not been the case.

For example, in his *Metabolism and Practical Medicine* von Noorden devotes but one page to the question of myasthenia in general, mentioning the work of Kauffmann, who has investigated myasthenia gravis, more especially in connection with the effect of fatigue upon the nitrogenous metabolism. Kauffmann concludes that with the appearance of fatigue there is a diminution in the output of urea coinciding with an increase in the output of ammonia. He regards this as indicative of an acid intoxication, and ascribes to lactic acid the poisonous role. Lactic acid was found in large quantities in the urine on the days of work, as

[1] Read June 2, 1909.

well as in the blood serum. In Kauffmann's case, as well as in two others reported by Mohr and Boldt, the liver was diseased, and, according to von Noorden, it seems as if the appearance of the myasthenia coincided with the extent of the intermediary products of metabolism.

Perhaps the most significant work on this subject is that of Spriggs, who has investigated the nitrogenous metabolism and the creatinin output in a variety of cases of muscular loss of function.

Spriggs finds that there is a decrease of creatinin in proportion to the decrease of muscle bulk; and that this holds true, though to a less degree, in myasthenia gravis, in which condition, however, there is, of course, little decrease of muscle volume.

When the case now under discussion was first considered with a view to chemical study, general metabolic investigations of the above nature were contemplated on the basis of there having been so little attempted in this connection; but at the suggestion of Dr. D. L. Edsall there were included examinations of the calcium, and magnesium metabolism, the former of which afforded the findings of most interest.

Jacques Loeb and his associates showed a few years ago, that certain agents, when injected into the economy, cause precipitation in an insoluble form of the body calcium and produce a condition of muscular spasm. This condition could be induced by him with all the alkaline earths, except barium, and could be relieved by agents which induce the re-solution of the precipitated calcium salts or by a further injection of calcium. Meltzer and Auer have shown that rigor mortis is hastened by the injection of calcium and under certain conditions of magnesium salts as well; and have also called attention to the great toxicity of magnesium salts when injected into animals, even in minimal amounts. They have shown, furthermore, that there exists between calcium and magnesium an apparent antagonism, whereby animals rendered nearly moribund by magnesium can be resuscitated immediately by minimal injections of calcium.

In somewhat the same line the work of MacCallum, Voegtlin,

and Halstead indicates that there exists an intimate relation between tetany and calcium metabolism. In persons the subject of extirpation of the thyroid for goitre, in whom the parathyroids have also been inadvertently removed, and in dogs in which this procedure has been experimentally performed, there occurs a loss of calcium in the urine and feces. The muscle spasm, increased respiration, and other phenomena characteristic of tetany, however, which follow upon removal of the parathyroids, can be controlled and indeed prevented by the administration of calcium salts in amounts sufficient to compensate somewhat for the loss sustained.

Such observations as the above rendered reasonable the investigation of the calcium and magnesium metabolism in myasthenia gravis in the hope of observing some relation between it and the perverted muscular functions of that condition.

The case under observation was that of an extremely intelligent man of about fifty-five years of age, presenting well-advanced features of the disease. His previous history is without special significance, and the course of the disease need be mentioned only in so far as to state that it was in some slight degree amenable to diet and hygienic treatment. The intelligence of the patient and his coöperative efforts made possible accurate study upon him, and the subjective evidence advanced by him has been of value throughout, as an index of his progress for better or worse.

He was placed for ten days upon a metabolic diet whose content in the various features investigated either was known or could be easily determined. The features investigated were the total nitrogen, ammonia, creatinin, calcium, and magnesium, all of which were determined in the urine; while the feces were examined for total nitrogen, calcium, and magnesium. Articles of his diet in which the calcium and magnesium content were not known, were submitted to similar investigations.

The methods adopted were the Kjeldahl in the determination of nitrogen and Folin's colorimetric method in the determination of creatinin. The calcium was determined as oxide, after precipitation by ammonium oxalate and subsequent ignition; the

magnesium, as oxide, after precipitation with ammonia from the calcium filtrate and subsequent ignition. During the experiment the patient was maintained, as far as possible, under the same circumstances as those under which he had been living just prior to it.

Under the conditions of the dietary administered the present case did well. The determination of the nitrogen balance over a period of six days of the seven days studied showed a nitrogen retention of about 16 grams (16.6117). In this period of six days, however, the calcium metabolism not only failed to keep pace with the nitrogen retention, but did not even maintain an equilibrium, showing, indeed, an actual loss amounting to more than 8 grams (8.4888).

Investigation of the magnesium metabolism showed no apparent departure from the normal. The ammonia output was apparently also well within the limits of health, and no indication of an acid intoxication could be induced therefrom.

Folin's observations have suggested that the creatinin output in any individual is a constant, independent of muscular exercise. Shaffer believes that in pathological subjects the creatinin is usually low, although the creatinin coefficient ($\frac{15}{24}$ per kilo body weight) shows a direct parallelism with the muscular efficiency of the individual; and indicates, furthermore, some special process of normal metabolism taking place largely, if not wholly, in the muscles. The investigations of Spriggs on the creatinin output in several of the primary myopathies, in myasthenia gravis, myotonia congenita, and tabes dorsalis, essentially corroborate this finding, and this worker believes creatinin to be a product of the internal structural metabolism of muscle and not of its contraction.

In a normal individual, Spriggs found the output of creatinin nitrogen expressed in percentage of total urinary nitrogen to be 3.9 per cent.

In his series of pathological cases, the creatinin nitrogen as percentage of total nitrogen was as follows:

Normal woman	3.9
Progressive muscular dystrophy (boy of 15½ yrs.)	0.8
Progressive muscular dystrophy	1.7
Tetanus	4.0
Tetanus	2.2
Spastic paraplegia	3.7
Spastic paraplegia (dementia paralytica)	4.2
Myasthenia gravis	3.0
Amyotonia congenita (boy of 4½ yrs.)	0.3
Healthy boy (4½ yrs.)	1.0
Locomotor ataxia	3.9

The present case showed an average daily output of creatinin of 0.59155 gram, which is slightly below the low limit of excretion in health and also below the figures in Spriggs' case of myasthenia (0.689 gram). Expressed in terms of creatinin N. as percentage of the total urinary N., however, the output was only 1.67, which is considerably lower than the same quotient in the case just mentioned.

Spriggs deduces from his work that in myasthenia gravis there is a diminution in the creatinin output which should be taken to indicate a connection between the excretion of creatinin and muscular function apart from bulk. The present case gives color to this view, and shows, further, that the decrease may be even more marked than that which his case showed, and, indeed, sometimes almost as great as occurs in primary myopathies with loss of muscle substance.

This would seem to suggest that myasthenia gravis is a disease of disturbed internal muscular metabolism *per se*. This finding is peculiarly in consonance with the observed loss of calcium; which element is as above stated, in such close connection with the functions of muscular activity. The relation seems to be more than accidental, and calls for further investigation.

As far as can be ascertained this study forms the only attempt at a determination of the calcium metabolism in myasthenia gravis; and while one case affords insufficient grounds for positive conclusions, it is at least suggestive that, in view of the very intimate relation existing between some of the alkaline earths and muscular activities, there should be observed in this instance so distinct a loss of calcium salts. The case has remained under

the observation of Dr. W. G. Spiller, who has administered calcium lactate over a considerable period of time. Other remedial measures have been ordered, including the use of strychnine; but whether because of the calcium administered or by way of coincidence alone, the patient has markedly improved in the course of the year and a half since the observations above mentioned, and the establishment of the calcium therapy. Remissions of long periods have been reported by several observers in the course of myasthenia gravis, but, at least, they are rare, and it may well be that we have in this definite indication of disturbed metabolism a clue to practical therapy in this disease.[1]

Through the kindness of Dr. Spiller, opportunity has been afforded for the examination of another case of myasthenia gravis with the same objects in view; but the patient was too refractory to allow of proper control of her diet, and conclusions based upon this study would be unwarranted, except in so far as to state that the results suggested no radical departure from the conditions above described.

Finally, I wish to express great obligation to Dr. W. G. Spiller for the opportunity of studying the case, and also to Dr. D. L. Edsall for his suggestions and assistance during the course of the determinations.

Conclusions. The above study indicates that in myasthenia gravis there may be marked loss of calcium by the tissues even under circumstances of marked nitrogen retention.

The creatinin output in myasthenia gravis may be reduced to a point below normal; the output of creatinin N. expressed in percentage of the total urinary N. may be almost as low as that seen in conditions of true muscular wasting.

These facts taken together form a reasonable basis for belief that myasthenia gravis is a disease of deranged muscular metabolism, and that one at least of these two factors (viz., the loss of calcium) may stand in such a causal relation as to indicate the therapeutic administration of that element.

[1] In a later report the patient says that for the first time since his illness began he feels that his complete recovery is possible and not far distant.

Day.	Amount.	Creatinin.	Creatinin N. as per cent. of total urinary N.	Total N. in urine.	NH_3.	NH_3 N. as per cent. of total urinary N.	Ca.	Mg.
	c.c.	Grams.	Per cent.	Grams.	Grams.	Per cent.	Grams.	Grams.
24	1550	0.6448	1.990	11.8876	1.0961	5.470	0.4500	0.2859
25	1390	0.6258	1.700	13.4848	0.7235	4.410	0.5054	0.2533
26	1415	0.5387	1.567	12.6266	0.5522	3.600	0.5515	0.1714
27	760	0.5476	1.840	10.9318	0.6610	4.055	0.4371	0.2639
28	1235	0.4281	1.230	12.7350	0.8500	5.410	0.4379	0.2906
29	1645	0.6654	1.550	15.7514	1.0322	5.390	0.5433	0.2605
30	1906	0.7437	2.120	12.8532	0.6566	4.207	0.5862	0.2840
Urin'y totals		3.5493	Av., 1.668	78.3828	4.4755	Av., 4.5116	3.0714	1.5237

Ca. in feces . . . . . 18.6051 grams
Mg. in feces . . . . . 0.7257 grams
N. in feces . . . . . 4.9156 grams

Sum total of output:
Creatinin . . . . . 3.5493 grams
Total N. . . . . 83.2984 grams
Total NH_3 . . . . . 4.4755 grams
Total Ca. . . . . 21.6765 grams
Total Mg. . . . . 2.2514 grams

Average diet[1] consisted of:

Breakfast:
Eggs . . . . . 90 grams
Bread . . . . . 50 grams
Milk . . . . . 420 c.c.
Butter (for day) . . . . . 40 grams

Dinner:
Eggs . . . . . 90 grams
Bread . . . . . 50 grams
Milk . . . . . 420 c.c.
Rice . . . . . 30 grams

Supper:
Eggs . . . . . 90 grams
Bread . . . . . 50 grams
Milk . . . . . 420 c.c.
Apples . . . . . 130 grams
Sugar . . . . . 32 grams
Salt . . . . . 5 grams

[1] In order to save space the diet tables are not given entire, but the balance was made up on the actual totals and not on the basis of an average day. The percentage content in Ca. and N. of eggs, bread, milk, rice, and butter is taken from "A Contribution to the Chemical Pathology of Acromegaly," by Edsall and Miller, University of Pennsylvania Medical Bulletin, vol. xvi, p. 143.

Total food consumed in six days:

Eggs	1719 grams
Bread	1050 grams
Milk	8340 c.c.
Rice	210 grams
Apples	910 grams
Butter	280 grams
Salt	30 grams
Sugar	210 grams

Total grams of Ca. and N. in intake of food:

Ca.	13.1877 grams
N.	99.9101 grams

Positive[1] N. balance of	16.6117 grams
Negative Ca. balance of	8.4888 grams

[1] The balance was made up on the last six days, as there was some discrepancy in the diet figures for the first day. As a matter of fact, however, this discrepancy could be safely disregarded and the amount ingested for that day assumed as practically identical with those following, as the figures are in perfect accord. This makes the metabolism studies cover, essentially, a period of seven days, one more than that actually considered. The magnesium output was so obviously within normal limits that a balance was not computed.

SPASM OF THE ARTERIES.[1]

By PAUL LAZARUS, M.D.

(Translated and Abstracted by A. A. ESHNER, M.D.)

Professor Lazarus began by saying that he chose to deal with functional disorders in contradistinction from anatomical alterations in the bloodvessels. He pointed out that under ordinary conditions the circular muscle fibers of the arteries predominate in action over the longitudinal fibers, thus maintaining the normal vascular tone. This may be varied by influences acting from without or from within. In consequence of irritable weakness resulting from divers abnormal conditions, the muscular fibers of the bloodvessels become unduly sensitive, and accordingly they react in an abnormal manner to various stimuli. The vasomotor neuroses comprise a large number of disorders: for example, migraine, exophthalmic goitre, sclerodactyly, scleroderma, Raynaud's disease, erythromelalgia, acroparesthesia, Stokes-Adams syndrome, paroxysmal hemoglobinuria and hematuria, vasomotor ataxia. By some observers the painful crises of locomotor ataxia are attributed to spasm of cerebral or spinal arteries. Professor Lazarus divided vasomotor disorders into two types, namely, hypertonic and hypotonic. He said that depressing influences, especially of an emotional character, have a tendency to lower vascular tone, while pleasant impressions have the opposite tendency. He cited the case of a woman in whom a constant increase of blood pressure of apparently functional origin finally eventuated in the development of arteriosclerosis. He spoke of,

[1] Read October 6, 1909.

and passed about pictures showing, a condition in which in consequence of emotional shock due to the occurrence of an apoplectic seizure in a parent there developed in a woman persistent pallor in one digit, then in others, and finally atrophy and gangrene in parts supplied by arteries derived from the arch of the aorta, while the lower portion of the body developed a condition simulating acromegaly, with manifestations of hyperemia. In conclusion he said he could conceive of no functional disturbance without circulatory or nutritive change. Mosso had demonstrated experimentally that every form of physical and cerebral activity is attended with nutritive or vascular changes in the brain, and he said then how much greater must be the result in connection with disordered action of the vasomotor system. Dr. Lazarus summarized his results by dividing angioneuroses into hypertonic and hypotonic forms, as well as mixed forms, in which he includes the form of disorder that Dr. Cohen has described as vasomotor ataxia, with vascular contraction at times, and dilatation at other times, the most common being the angiospastic variety. This may result in consequence of internal irritation through the heart or the blood or the wall of the vessel. It may also be due to irritation of the vasomotor tract from its origin in the cerebral cortex to its termination in the wall of the vessel. Accordingly, there may be various forms of arterial spasm. Arterial spasm may result in consequence of influences exerted through reflex action from the cerebral nerves, mental activity, the nerves of special sense, and the internal organs. Vasomotor emotional influences must be looked upon as compensatory of changes in the cerebral bloodvessels.

DISCUSSION.

Dr. S. Solis Cohen: This admirable and unusual paper should not be allowed to go without a word, however inadequate of application, as well as thanks. Personally it has been a satisfaction to me to have heard from the mouth of Professor Lazarus, as from the pens of Dr. Hertz and other European observers, confirmation of certain observations which I think some of my friends have been good enough to call a "fad," but which appeared to the observer to have considerable clinical significance. There seem to

be three elements in the origin of vasomotor disorders: (1) A constitutional liability of the patient; (2) an exciting cause, usually emotion, thermal change, or a toxic agent of endogenous or ectogenous origin; (3) the point which to me is most obscure—a local determent. Just why the same patient should have at one time migraine; at another a condition simulating hepatic colic; at another hemianesthesia or asthma or urticaria, or circumscript edema of the skin or mucous membranes, is yet to be determined. In some instances, as we can demonstrate by tracing with a probe upon the skin, a very slight mechanical force, scarcely to be termed trauma, determines it. At other times the exciting agent, a toxin or thermal change, acts locally, as when the hand plunged into ice water exhibits Raynaud's phenomena, or intestinal fermentation gives rise to enteralgia. But why, as in a case I showed Professor Lazarus today, a patient who has recovered from Graves' disease should be troubled with recurrent spasm of the temporal artery so that we can see the vessel become more distended and more tortuous above the point of constriction, this being accompanied with intense pain which lasts for a minute or two, and which can be relieved immediately by the administration of nitroglycerin to relax the spasm—or why, as in another case I exhibited to our guest, hemoglobinuria follows application of ice to the loins, or to the feet—I do not know; but evidently there is a local determent in each case. The important point is that we should diagnosticate the individual rather than the attack. The attacks vary; the individual remains the same. Whether that individual shall have one diagnosis to carry through life—a diagnosis which permits the patient to be helped, now and then, or get a new diagnosis from each physician to whom he applies in vain, seems a not unimportant matter.

I want, further, to express my own indebtedness to Professor Lazarus for reporting this extremely interesting case in which he has seen what I have indicated and asserted to be probable, the actual development of organic lesions from a disturbance of emotional origin. Some of my own patients whom I have observed for over twenty years have eventually died as predicted, from angina or apoplexy, consequent upon arteriosclerosis, but that the arteriosclerosis was present from the beginning I can never believe. I look upon it as the result of the continual strain to which the vessels have been subjected during life in consequence of the aberrant functioning of the neurovascular system.

GRAIN ITCH (ACARODERMATITIS URTICARIOIDES).

A STUDY OF A NEW DISEASE IN THIS COUNTRY.[1]

By JAY FRANK SCHAMBERG, M.D.

In the late spring of 1901 there appeared in Philadelphia and its vicinity an unfamiliar eruptive disease, occurring chiefly in household epidemics, which attracted the attention of the various skin specialists of the city. Having had an opportunity of studying about a dozen of these cases, I published in the *Philadelphia Medical Journal*, July 6, 1901, several photographs of the disease and a brief description under the title, "An Epidemic of a Peculiar and Unfamiliar Disease of the Skin." Since 1901, cases of the same character have been encountered each year in Philadelphia, usually between the months of May and the beginning of October. The cause of the disease remained obscure and undetermined despite careful interrogations designed to ascertain the cause of the affection and the explanation of the household epidemicity.

In the spring and summer of 1909 this peculiar eruptive disease became quite prevalent in Philadelphia and neighboring towns. An outbreak among twenty sailors upon a private yacht docked in the Delaware River attracted the attention of both the city and the Federal health authorities. The Surgeon-General of the United States Public Health and Marine Hospital Service delegated Dr. Joseph Goldberger, Passed Assistant Surgeon, to proceed to Philadelphia to make an investigation of the disease. Being already engaged in a semi-official study of the outbreak

[1] Read November 3, 1909.

myself, Dr. Goldberger and I concluded to continue the inquiry jointly.[1]

After carefully examining the twenty sailors who had been sent to a hospital, we visited the yacht whence they came and made a searching examination of the conditions on board. Our attention was directed to the fact that a number of new straw mattresses had been received, and that the disease was confined to those who had slept upon these mattresses or had placed their clothes upon them. Eleven officers and members of the crew who did not sleep upon the new mattresses remained entirely free of the disease.

At about the same period information was received concerning an eruptive disease prevailing among the sailors of four other boats plying along the Delaware River. Investigation disclosed the fact that these boats had also received new straw mattresses, and, furthermore, that only those were attacked who slept upon the mattresses or otherwise came in contact with them.

In addition to these cases among sailors, we examined or received authentic information concerning seventy other cases of this disease occurring in twenty different households in Philadelphia and its vicinity.

In practically every instance we were enabled to determine that the patient had either recently slept upon a new straw mattress or had freely handled the same. Where only one person in a household was affected, it was found that he was the only one to occupy a bed supplied with a new straw mattress. We were able to trace all of the incriminated mattresses to four leading mattress manufacturers.

Careful investigation warranted us in excluding from consideration the ticking of the mattresses and the jute or cotton topping contained therein. The cause of the disease was, therefore,

[1] The result of this investigation was published by Drs. Goldberger and Schamberg in a preliminary report entitled "Epidemic of an Urticarioid Dermatitis due to a Small Mite (Pediculoides Ventricosus) in the Straw of Mattresses." Public Health Reports, United States Public Health and Marine Hospital Service, July 9, 1909, xxiv, No. 28.

circumscribed to the straw. Repeated inquiries elicited the information that all of the manufacturers had received, at the time the disease-producing mattresses were made up, wheat straw from a dealer in Salem county, in southern New Jersey. One manufacturer had used straw from this source exclusively in the infected mattresses.

Finding of a Parasite. Dr. Goldberger and the writer sifted the straw from a mattress through the meshes of a fine flour sieve upon a large plate glass over white paper. Close scrutiny of the siftings under strong electric illumination soon detected some slight motion. The moving particles were touched with a needle moistened in glycerin and transferred to a glass slide. Search with the microscope disclosed the presence of a mite of very minute dimensions. This mite was identified for us by Mr. Nathan Banks, expert in acarina, of the United States Bureau of Entomology, as very close to, if not identical with, the Pediculoides ventricosus. In order to demonstrate experimentally the etiological relationship of the suspected straw mattresses, Dr. Goldberger exposed his bared left arm and shoulder for one hour between two mattresses. At the end of about sixteen hours a number of characteristic lesions appeared upon the arm, shoulder, and chest. Later, three volunteers slept upon the mattresses, and each one developed the eruption at the end of about the same period.

Dr. Goldberger later took some of the sifted straw, divided it into two portions, and placed it in two clean Petri glass dishes. One of these was applied for one hour to the left axilla of a volunteer. At the end of sixteen to seventeen hours the characteristic eruption was present in the area of the left axilla to which the Petri dish of straw siftings had been applied.

The second portion of the straw siftings in a Petri dish was exposed to the vapor of chloroform under a bell jar, with a view to killing any insect or acarine that might be present. These siftings were then applied to the right axilla of the same volunteer to whose left axilla the untreated siftings had been applied. The chloroform evidently destroyed in the siftings the agent

that was producing the eruption, for no lesions appeared after the application of the chloroformized siftings.

Dr. Goldberger further fished out of some straw siftings five minute mites, and, placing them in a clean watch crystal, applied the crystal to the axilla of another volunteer. At the end of about sixteen hours following this application five of the characteristic lesions appeared on the area to which the mites had been applied.

Eruption. The disease is characterized by an eruption consisting of wheals, many of which exhibit at their summits a central pinpoint- to pinhead-sized vesicle. This is the peculiar lesion of the disease, and is so characteristic as to immediately suggest this affection. The contents of the vesicle are clear but for a brief period of time, and then become lactescent or distinctly puriform, constituting a well-marked pustule. Instead of frank wheals, the efflorescence may consist of barely elevated, erythemato-urticarial spots or papulo-urticarial lesions. The latter are edematous in character, but have the size and shape of papules. The lesions generally vary in size from a lentil to a fingernail, and are rounded, oval, or irregular in shape. They are edematous, like the wheals of ordinary urticaria, and are not infrequently elevated 1 to 2 mm. above the level of the skin. The color is usually a warm rose tint; only rarely do the lesions exhibit the pinkish white anemic area seen in ordinary "hives." The central vesicle or pustule is usually minute, not exceeding in diameter 0.5 mm.; in many cases it is pinhead in size (about 2 mm.); exceptionally the vesicle or pustule may reach a diameter of 3 mm. In such cases, the large vesicle situated upon an erythemato-urticarial base presents a strong resemblance to the lesions of chickenpox. In many patients the tops of the lesions are so excoriated by scratching that no vesicles are seen; instead, the wheals are surmounted by punctiform, dark red blood crusts.

The eruption varies in extent in different subjects; usually it is profuse, involving the neck, chest, abdomen, and back, and in a lesser degree the arms and legs. The greatest number of lesions is observed upon the trunk. The face is often free, although

at times scattered lesions are present. The hands and feet are nearly always exempt. The extent of the eruption and the size of the individual lesions are apt to bear an inverse relation to each other. In the most profuse eruptions, 10,000 or more lesions may be present.

In rare instances, the eruption may undergo modification and take on the characteristics of the macular type of erythema multiforme. I noted this especially in the sailor patient shown in photograph. The eruption on the face in this man was profuse, and there was an erythema involving both of the lower eyelids. In another patient there was, in addition to the usual eruption, a partial scarlatinoid rash involving the anterior and lateral surfaces of the chest. This patient had fever, nausea, chilliness, and vomiting.

There are, therefore, three varieties of the eruption; in the order of their frequency they are: (1) Urticaria vesiculopustulosa type; (2) varicelloid type with large central vesicle or pustule; and (3) erythema multiforme type.

The eruption is usually accompanied by the most intolerable itching. This is worse at night, and seriously interferes with sleep. The itching leads to violent scratching, with the consequent production of excoriations and blood crusts, and at times pyogenic infection of the skin.

Systemic Symptoms. During the early days of the attack the patient may experience chilliness, and in some cases nausea and even vomiting. Mild rigors may recur throughout the course of the next few days. The temperature may be elevated from 100° to 102° F., or higher, with corresponding acceleration of the pulse rate; this pyrexia may continue for several days. It is, however, a very variable symptom, and is often lacking. Some patients, although afebrile, complain of malaise and anorexia; others do not admit being ill at all. Indeed, even the patients with some elevation of temperature are not inclined to seek their beds. There is at times a moderate enlargement of the superficial lymphatic glands.

Blood Examinations. The twenty sailors previously referred to were treated in the Marine Hospital Wards of St. Agnes' Hospital. The resident pathologist of the institute, Dr. John Albert Kolmer, made, at my suggestion, careful examinations of the blood. A summary of Dr. Kolmer's report is herewith subjoined:

Summary of Blood Examinations. June 8: Leukocytes, 8245; small lymphocytes, 27.7; large lymphocytes, 7.95; transitionals, 1.01; polymorphonuclears, 58.12; eosinophiles, 4.9; mast cells, 0.22. June 12: Leukocytes, 7470; small lymphocytes, 29.03; large lymphocytes, 6.63; transitionals, 1.12; polymorphonuclears, 59.99; eosinophiles, 2.56; mast cells, 0.37.

Two examinations were made in each case. Due care was exercised in avoiding digestive leukocytosis. Wright's stain was used throughout. In each case two smears were examined at every examination.

One must examine the tables and not the averages to appreciate the blood changes. Tentative examination will show:

1. That a moderate leukocytosis was present in most cases during the acme of the disease.

2. That the eosinophilia was well marked in the larger number of cases at the height of the eruption.

3. Both the leukocytosis and eosinophilia subsided with improvement of the symptoms.

4. That the other leukocytic elements show no particular changes.

The urine was examined on two occasions by Dr. Kolmer. Albuminuria was present in three cases. A more recent contributor to this subject, Dr. Lyman T. Rawles, of Huntertown, Indiana, has also noted albuminuria in several of his patients. This condition is probably analogous with the albuminuria which not infrequently accompanies scabies. Nicholas and Jambon found albumin in the urine sixteen times in 100 cases of scabies.

Production of the Cutaneous Lesions. Unlike the scabies mite, the pediculoides does not burrow into the skin. Microscopic examination of vesicles and pustules has demonstrated the absence of the mite or any part thereof beneath the surface

of the skin. The probabilities are that the pediculoides in the process of extracting nourishment from the skin, synchronously injects an irritant substance which gives rise to the lesions.

Upon this phase of the subject, Laboulbene and Megnin, quoted by Moniez, say: "One cannot doubt that this acarus is endowed with a venomous saliva, the inoculation of which is principally the cause of the death of the larvæ and nymph insects on which it lives and multiplies. This saliva is secreted by four pairs of vesicles disposed along the esophagus and opening into the larynx. The emission of this saliva follows immediately upon the puncture by the mandibles acting as a lancet."

Diagnosis. The affection is apt to be confounded in different cases with one of three diseases—urticaria, chickenpox, and scabies. I have known many such errors to be made. In one case, with a particularly profuse eruption, the patient was under suspicion of suffering from smallpox.

The affection may be distinguished from ordinary "hives" by the longer duration of the individual lesions, by the central vesiculation, the constitutional disturbance, the greater persistence of the attack and the occurrence of the disease among groups of persons.

Chickenpox, which is at times quite closely simulated by the eruption, may be excluded by the duration of the disease, the smallness of the vesicle, the violence and persistence of the itching, and the great incidence of the disease among adults.

Scabies, or "itch," may be strongly suggested when the lesions are excoriated by scratching; it may be eliminated from consideration by the freedom of involvement of the hands, by the uniform eruption of erythemato-urticarial lesions surmounted by small vesicles, and by the distribution of the eruption.

Pediculosis corporis could be excluded by studying the character of the individual lesions and by the failure to find the pediculi.

The history of contact with straw is, of course, of great diagnostic value.

Treatment. As the pediculoides does not burrow beneath the skin, but merely perambulates upon the surface, it is a com-

paratively simple task to rid the patient of the parasites. Frequent warm baths with the use of soap would doubtless suffice. I have found the following ointment especially efficacious, as it not only destroys the mites, but also relieves the cutaneous symptoms: ℞ Beta-naphthol, gr. xxx; sulphur. præcip., ℥j; adipis benzoat., ℥j.

In order to prevent reinfection of the patient, his clothing should be disinfected either by boiling or careful sulphur or formaldehyde fumigation. Where the source of the parasites is a straw mattress, the latter may be rendered free of the mites by exposure in a closed chamber to steam, sulphur fumes, or formaldehyde.

Ordinarily the itching will subside within twelve to thirty-six hours, and the eruption will disappear in a week or ten days. Where, however, the cause is not recognized, and the use of the mattress is continued, I have known patients to suffer severely for periods varying from three to seven weeks, when gradual recovery would take place. It would seem, therefore, that the mite dies after a time and permits the patient to get well.

It should be remembered that the disease may be contracted from straw used for other purposes than mattresses. Patients have acquired the disease from straw used for packing purposes, from straw used under carpets, from contact with plants mulched with straw, etc. Sacks of infected wheat, barley, and other grains have likewise given rise to the disease.

Recapitulation and Conclusions. 1. An eruptive disorder, new to the physicians of this country, has since 1901 been appearing in the vicinity of Philadelphia, and within recent years also in Indiana, Ohio, and other States.

2. The disease is characterized by a widespread urticarioid eruption accompanied by intense itching and commonly by mild fever and other systemic symptoms.

3. The characteristic cutaneous lesion is a wheal surmounted by a minute vesicle which rapidly becomes pustular.

4. Nearly all of the patients exhibit a slight leukocytosis and a moderate eosinophilia, and a certain proportion have albumin in the urine.

5. Microscopic examination of the cutaneous lesions demonstrates that the mite does not burrow into the skin, as does the acarus of scabies. The pathological changes in the skin are characteristic of the lesions of urticaria.

6. The disease is due to contact with cereals or straw infected with the Pediculoides ventricosus or an allied species of mite.

7. Straw mattresses appear to give rise to the most severe and most persistent dermatitis, for obvious reasons. Straw used for packing purposes, and sacks of wheat, barley, and other grains constitute additional sources of infection.

8. The Pediculoides ventricosus has always been found associated with and predatory upon other insects, particularly grain-destroying insects.

9. The Pediculoides ventricosus has an economic and agricultural importance, because it tends to protect the grain crops by destroying the larvæ of the wheat straw worm, the joint worm, and the grain moth.

10. Wherever "grain itch" is prevalent it will probably be found that grain-destroying insects abound.

11. A similar or identical affection from contact with sacks of barley and wheat was noted by naturalists many years ago in France, Germany, Russia, and certain other European countries.

12. "Grain itch" is readily cured if the sufferer can avoid the source of infection.

DISCUSSION.

DR. M. B. HARTZELL: Those of us in this city especially interested in diseases of the skin began to see this affection some seven or eight years ago, and we all recognized that it was something which we had not met before, a distinct morbid entity whose cause we were ignorant of. When our attention was first called to it there was a small epidemic prevalent, which disappeared as suddenly as it had appeared. We saw no more of it until the following summer, when the cases were more numerous than in the previous season. As before, it disappeared quite suddenly. As Dr. Schamberg has stated, the disease presented some of the clinical features of urticaria, and very frequently it resembled more or less closely varicella, so that we gave it the provisional name of "urticaria varicelloides."

It was very curious that, in my own experience at least, very few children

were seen with this eruption, fully 90 per cent. of the cases being adults; and strangely, too, no relapses were observed; when the patients got well they remained well.

The affection seemed to run a self-limited course, and was very little influenced by treatment, which was therefore directed chiefly to the relief of the atrocious itching, which was one of the most prominent subjective symptoms of the disease.

Dr. Frank Crozer Knowles: I have seen between 35 and 40 cases of this condition at the skin dispensaries of the Pennsylvania, Howard, Children's, and University Hospitals. Some of these cases were epidemic in certain families; in one family there were four patients. Among the points which I would emphasize are the intense itching which occurred particularly at night, and the fact that the disease appeared during the summer months. The hands and feet were practically free. In the treatment the germicides seemed to answer the best purpose; sulphur and beta-naphthol are probably the most efficacious, and answered very well in many of the cases. The disease runs an acute course. The eruption usually comes out all at once and seems to be self-limited.

Dr. Schamberg, closing: I agree with Dr. Hartzell that relapses are rarely observed in this affection. However, one of the sailors referred to entered the hospital a second time with a most widespread eruption. He had left the bed infested with the mites, but later slept upon the same mattress and contracted the disease again. It has been stated that the disease is more or less self-limited; this appears to be true, although the cause of the self-limitation cannot be explained until we know more of the life history of the mite. I believe that after a time the mite dies in the straw, and thereafter the patient gets well. Before we knew the nature of this disease, I observed cases that lasted as long as seven weeks, the patients suffering the keenest distress from the intolerable itching. The use of germicide ointments are helpful and sometimes curative, but in other cases they appear to have but little effect. Since the cause of the disease has become known, it has been found that frequent bathing will suffice to cure the disease, provided the patient does not again come in contact with the mattress. From microscopic examination of some of the lesions we are enabled to definitely state that the mite does not burrow into the skin as does the parasite of scabies, but that it merely punctures the skin and sucks the nutritive juices. It doubtless at the same time injects a poisonous saliva. The disease has not yet been given a scientific name. As a popular name, "grain itch" would seem to answer all purposes. Years ago in France some of the cases were referred to as "grain fever." I would suggest the name "Acarodermatitis Gramenogenica" as appropriate. This would indicate an inflammation of the skin due to a mite having its origin in grain.

THE DIAGNOSIS AND SURGICAL TREATMENT OF ACUTE PANCREATITIS.[1]

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The diseases of the pancreas are, at the present time, being subjected to an ever-increasing amount of clinical observation and to experimental research of the most varied forms. Especially is this true of acute pancreatitis, a disease which in its several varieties touches upon some of the most important problems with which the abdominal surgeon and the physiologist of today must deal. Acute pancreatitis is a rare disease, although close study reveals the fact that many cases must in former times have been overlooked. It presents difficulties in diagnosis and treatment, and it is but rarely that either the surgeon or the medical man has the opportunity of seeing a large series of cases. I consider myself fortunate in having had the opportunity of observing closely several, and of operating on six cases. These are as follows:

Case I.—A white male, aged forty-four years, in the early part of 1901 suffered an attack of epigastric pain, lasting three hours and followed by diarrhœa. Pain recurred about every six months, was cramp-like in character, and relieved usually by mustard plaster. From 1901 to 1902 he felt very well, but afterward had pronounced symptoms of indigestion, loss of appetite, vomiting, belching of gas, and paroxysmal pain in the region of the stomach. During the week previous to the last attack the abdomen was distended, there was constipation, and

[1] Read November 3, 1909.

some yellowness of the sclerotics. The diagnosis by his attending physician was intestinal obstruction. Operation showed acute inflammation of the pancreas, which I believe supervened upon a chronic pancreatitis. The gall-bladder was drained, but no stones were found. The patient recovered and is perfectly well at the present time, having had no further trouble referable to the abdomen.

Case II.—White, male, aged forty-two years, admitted to the German Hospital, November 11, 1902.

The patient's past medical history is negative, except for occasional attacks of indigestion. His general health is good, but for the last twenty-five years he has had attacks of pain in the epigastrium lasting three to four hours, and accompanied by jaundice. No history of constipation was noted. Three days before admission he was seized with abdominal cramps, and the next day had epigastric pain and vomiting associated with much belching. Bowels did not move. On admission the patient was suffering with violent paroxysms of epigastric pain, was belching frequently, and vomiting. The vomitus was a clear, green, bile-stained fluid. The patient's bowel movements while in the hospital were clay-colored.

Physical examination showed the presence of slight icterus. The abdomen was markedly distended and tympanitic, the distention being most marked in the epigastric region. The *x*-ray examination showed the excursions of the diaphragm to be somewhat limited, and revealed a shadow in the region of the pancreas. The temperature on admission was 102.8° F., the pulse 104, and the respirations 30. The leukocyte count, November 14, was 8200, and on November 21, 13,850, with 81.3 per cent. of polymorphonuclears. The stools showed free fat. There was no glycosuria at any time.

The patient appeared to improve somewhat. The pulse dropped to between 86 and 96 to the minute; the respirations to 24, and the temperature to between 99.6° and 101° F. before the operation.

On November 22, 1902, the patient was operated upon, under ether narcosis. The incision was made through the upper portion

of the right rectus. Some fat necrosis of the gastrocolic omentum was found. The gastrocolic omentum was opened, exposing the pancreas, which was found to be diseased, with the head of the gland thickened. Some hemorrhage was present. The pancreas was drained at the site of the hemorrhage with a rubber tube, around which was packed sterile gauze. Death occurred soon after the operation.

Autopsy. The preperitoneal fat and all the fat in the abdomen, omentum, and mesentery was studded with little areas of fat necrosis. The pancreas was much diseased. The tail was gangrenous and surrounded by a reddish, purulent fluid. The head and body of the organ had remained relatively normal. The lesser peritoneal cavity contained much purulent, reddish-yellow fluid, containing broken-down pancreas. The gall-bladder was full of calculi, but it was impossible thoroughly to examine the biliary ducts owing to adhesions and necrosis. About the sloughing gangrenous pancreas there were adhesions; but there was no general peritonitis.

The salient features of this case, to which I shall refer more in detail in the general discussion, are: (1) General abdominal distention, most marked in the epigastrium; (2) the presence of biliary vomiting and frequent belching; (3) the drop in pulse rate, respiration, and temperature, with improvement in the patient's general condition, after the severe initial symptoms; (4) the presence of fat necrosis; (5) the presence of biliary calculi; (6) the involvement of the tail of the pancreas almost exclusively; (7) the presence of free fat in the feces and the absence of glycosuria; (8) the absence of free fluid in the abdomen; and (9) the mistake of not opening the lesser peritoneal cavity through the left loin posteriorly, instead of transperitoneally.

Case III. – C. K., white, female, aged sixty-one years. Admitted to the German Hospital, January 20, 1905.

The patient was admitted with the diagnosis of acute intestinal obstruction, and was operated upon immediately. No history was obtainable. On admission the pulse was 76 to the minute and the temperature was 99° F.

Under ether narcosis an incision was made in the left inguinal region, in the belief that the sigmoid was at fault. The descending colon and sigmoid were examined and found normal, and the original wound was closed. The abdomen then was opened in the median line, the incision extending from the ensiform to the pubis. The entire intestine was searched for an obstruction, but none was found. At the greater curvature of the stomach near the pylorus a dense mass of adhesions was found, with hemorrhage beneath. The adhesions were separated and the pancreas was found hard, nodular, enlarged, and the seat of a large hemorrhage. Four pieces of gauze were carried to the head of the pancreas and a glass tube was placed in the pelvis. An antiseptic dressing was applied. The patient died fifteen hours after the operation.

Postmortem. The pancreas was 24 x 8 x 4 cm. in size and weighed 290 grams. It was dark red in patches, and densely adherent to the stomach and the transverse colon. Areas of fat necrosis were found in the surrounding tissues. The gall-bladder contained bile and about fifty stones; the ducts were patulous.

This was evidently one of those extremely acute cases of pancreatic hemorrhage, that is, hemorrhagic pancreatitis, referred to by some authors as fulminant. The operation took place within a day of the onset of the illness, even before fat necrosis had an opportunity to occur, yet the very severity of the disease rendered the prognosis hopeless. Especially to be noted is the diagnosis of acute intestinal obstruction. As will be seen on reading the case reports of this disease, this diagnosis is very commonly made—far oftener than the true one. We find in this case also: (1) Fat necrosis; (2) the presence of calculi; and (3) a very slow pulse rate—76—with a temperature of 99° F.

Case IV.—White, female, aged forty-one years. Admitted to the German Hospital, October 17, 1905.

No history of tuberculosis or malignancy was obtained. The patient had always had general good health. Nine weeks before admission she became gradually ill, complaining of pain in the

right side of the abdomen referred to the back, epigastrium, and right iliac fossa. Three weeks ago she had severe abdominal pain in the right side of the abdomen, but most severe in the upper portion. The pain was followed by vomiting and was almost constant. Some soreness in the upper abdomen was also noted. The nausea and vomiting had been more or less continued. On admission the patient's abdomen was distended, especially above the umbilicus. Rigidity of both recti muscles was noted, but most marked above the umbilicus on the right side. There was an indefinite mass in the epigastrium, which was moderately tender. On admission the temperature was 100° F., pulse, 76. While the patient was in the hospital the leukocytes varied from 8600 to 32,900, and the hemoglobin from 45 to 68 per cent. Free fat and occult blood were found in the stools.

Operation, October 18, 1905. Under ether narcosis, an incision was made in the median line above the umbilicus; the stomach was found distended and pus escaping through the foramen of Winslow. The wound was closed and a second incision made along the right costal margin, exposing the lower margin of the liver adherent to the stomach. The adhesions between the stomach and the liver were separated, and the gastrohepatic omentum was found to be thickened and edematous. An aspirating needle was passed through the thickened gastrohepatic omentum in the direction of the lesser peritoneal cavity, and blood and pus were obtained. A free incision was then made, allowing the escape of considerable pus. A rubber tube, surrounded with gauze, was then placed in the lesser peritoneal cavity. The gall-bladder was searched for but not found. After the operation the patient developed a septic temperature. The leukocytosis continued, and she left the hospital in poor condition, with a discharging sinus. She died after some weeks of continued sepsis.

In this case we may note particularly: (1) Gradual onset of the illness, indicative of a subacute suppurative process rather than an acute necrotic one; (2) continued vomiting; (3) low pulse rate—76 before operation; and (4) an indefinite mass in the epigastrium.

Case V.—White, male, aged twenty-seven years. Admitted to the German Hospital March 18, 1908.

One year before admission the patient had four or five attacks of abdominal pain, accompanied by jaundice. Two and one-half weeks before admission he had a severe attack of epigastric pain, accompanied by nausea and vomiting. The pain continued up to the date of admission, with frequent exacerbations. It started in the epigastrium, and was referred all over the abdomen, and to the back and shoulders. The patient has been jaundiced more or less ever since the onset of this attack.

On admission the patient was jaundiced, the respiratory excursions were limited, and the respirations short. The liver extended from the sixth interspace to two fingers' breadth below the costal margin in the mammillary line. There was slight epigastric fulness and spasticity of both recti muscles in this region. Some tenderness was noted over the entire epigastrium, and it was quite marked over Mayo Robson's point. The pain continued without relief up to the time of operation. The patient's temperature on admission was 98.4° F., and remained febrile during the entire course of the illness, but only for about three days after operation, with a maximum of 100.4° F. The pulse on admission was 88.

The operation was performed on March 21, 1908, under ether narcosis. An incision was made through the right rectus. The gall-bladder was found adherent to the colon and omentum, and contained calculi. Posterior to the stomach there was a soft fluctuating mass about the size of two fists, pushing the stomach forward. A finger placed in the foramen of Winslow found this to be in the position of the pancreas. The gall-bladder was walled off with gauze pads and aspirated; 40 c.c. of mucopurulent fluid was removed. This was sterile, as shown subsequently by culture. The gall-bladder was opened and four large and twenty-four small stones were removed from it and the dilated cystic duct. A tube drain was introduced into the gall-bladder, and it was sewed to the peritoneum. The choledochus was found to be patulous. The wound was closed and the patient

placed on his right side and an incision made in the left loin, extending down 7 cm. from the costal margin, and just external to the outer border of the erector spinæ. Within the fatty capsule of the kidney there was much fat necrosis. An abscess was evacuated in the location of the pancreas, and about half a liter of bloody purulent fluid escaped. The cavity was drained with a large rubber tube and two pieces of gauze.

The patient made an uneventful and practically afebrile recovery. The drain was left in the gall-bladder eleven days, and that in the posterior incision for several weeks, although the drainage gauze in this incision was removed in six days. The discharge from this wound was found to be very irritating to the skin.

The points of interest here are: (1) The slow pulse and afebrile course after operation; (2) the presence of biliary calculi; (3) the presence of fat necrosis around the abscess cavity; and (4) the irritating character of the pancreatic discharge.

Case VI.—H. M. N., a white male, aged thirty-nine years. Admitted to the German Hospital, December 28, 1907.

The case, which has been reported by Dr. Jurist,[1] was one of gangrenous pancreatitis, in which following a posterior incision purulent and necrotic material was removed from the region of the pancreas. Ten days after the operation and again a week later, large pieces of necrotic and gangrenous pancreas were discharged through the wound. Thereupon the patient's condition improved markedly, and eventually he made a perfect recovery. He now enjoys excellent health, his metabolism apparently is undisturbed, and he has no glycosuria.

Of special importance in this case are: (1) The primary shock with a slow pulse; (2) extreme prostration thereafter, with signs of profound toxemia; (3) the operation in the second stage; and (4) the use of the posterior incision alone.

In discussing this series of cases, it will be admitted that in each case there was an acute pancreatitis. It is true that they are of various types. Thus in Case II we have an example of

[1] American Journal of the Medical Sciences, 1909, cxxxviii, 180.

a slowly progressing type, of the hemorrhagic variety. This may perhaps be considered one of those cases in which the inflammation preceded the hemorrhage by some time, as the latter does not furnish the changes most marked pathologically, nor is the course that of an acute hemorrhagic case. Case IV represents the ultra-acute hemorrhagic pancreatitis of Mayo Robson's classification, in which the hemorrhage is the primary factor. The rapid course and extreme disorganization of the gland itself make this apparent. This represents that class of cases which is least promising for any form of surgical intervention—indeed, when the pancreatic disintegration has reached the stage which it had in this instance, it is almost hopeless to expect a recovery. Cases IV and V represent the acute suppurative variety of pancreatitis: not a localized abscess in the pancreas, but a more or less diffuse suppuration with involvement of the omental bursa. Case VI is of the gangrenous type. Doubtless this commenced as an acute necrosis also, probably hemorrhagic in type, which involved nearly all of the gland, as is shown by the extent of the gangrene. The subsequent well being and perfect assimilation of the patient would lead us to suppose that a portion of the head of the pancreas was entirely unaffected by the disease.

Etiology. As to the etiology of acute pancreatitis much has been written, largely from the standpoint of experiments. Clinically several factors have been mentioned. Many authors have called attention to the fact that people in whom acute pancreatitis is found are, as a rule, of middle age and inclined to stoutness. As regards the age, this would hold true in my cases, with the exception of Case V. In Cases II, V, and VI the patients were, however, very well developed, and not given to excess of adipose tissue. In Case VI, there was the history of a diabetic parent, perhaps only a coincidence, but nevertheless rather striking.

Opie[1] has called attention to the association of various forms of pancreatitis with gallstones, especially those situated in the choledochus. In Cases II, III, and V, I found gallstones, but

[1] Diseases of the Pancreas, 1905.

in no case obstructing the choledochus. In Case IV the gall-bladder was not found; it was so bound down by adhesions that the search for it in the presence of so much free pus, would have been dangerous. In Case VI the bile ducts naturally could not be inspected; but it seems reasonable to assume that stones were present, in view of the many attacks of pain resembling biliary colic.

Thus, in six cases of acute pancreatitis, four (67 per cent.) had gallstones. In two additional cases personally communicated to me which have recently occurred in this city, gallstones were not present. It is noteworthy that in the three cases in which gallstones were actually found there was no stone in the choledochus. I have a number of times found chronic pancreatitis associated with a stone in the common duct.

My experience as regards biliary calculi coincides with that of most authors. The investigations of Opie have already been mentioned. The only investigator of prominence who disagrees with these conclusions is Truhart,[1] who, in the analysis of a large number of cases, found that a smaller percentage of patients with acute pancreatitis had gallstones than those who died from other causes.

Fitz, Opie, and most American and British authors have inclined to the belief that the causative factor in acute pancreatitis is most often some form of infection, while Chiari and his school incline to the theory of a chemical autodigestive process. The experimental results of various investigators have differed greatly on this subject. While Opie, Fitz, and others, as mentioned, give great prominence to the factor of infection, Truhart, in an analysis of 74 cases of acute pancreatitis, found that in only 14 could microörganisms be demonstrated. Naturally this refers to the pancreatitis itself, for when pus has once formed and an abscess is present, this is likely to become secondarily infected. Then again, the fact that microörganisms cannot be shown by culture does not eliminate them as causative factors. In one case (V) bacillus coli was demonstrated in the pus.

[1] Pankreas Pathologie, Wiesbaden, 1902.

It seems reasonable to assume, however, when gallstones are present and not in the choledochus, that whatever causative action they may have had has been exerted by the concomitant infection. A curious feature in this connection is that in the case mentioned the apparently purulent fluid contained in the gall-bladder showed no bacteria, while the colon bacillus was found in the pancreatic abscess.

Case III is an example of those in which commonly no bacteria are found, and seems to be a case of primary hemorrhage into the pancreas.

Pathology. The pathology of acute pancreatitis has been the subject of much discussion, and bears an intimate relationship to the question of etiology. So far as my records go, there was nothing to throw any light on the presence of an autodigestive process, which so many German authors, notably Doberauer[1] and Guleke[2] have brought into the foreground as the initial process in acute pancreatitis. On the whole, I incline to the theory of infection rather than that of primary chemical change in the pancreas. So many substances act as stimuli to the disintegration of the pancreas by so-called autodigestion that it seems quite likely that bacteria can also do this. And, indeed, Hekma[3] furnished experimental proof of this fact.

Sailer and Speese[4] found that a toxic substance was present in the blood of dogs suffering from acute pancreatitis experimentally produced by the injection of sterile oil into the pancreatic duct followed by ligation of the duct. Williams and Busch[5] found "anatomical and experimental evidence that made it seem probable that some cases of acute pancreatitis may be caused by regurgitation of duodenal contents into the diverticulum of Vater, the way having been opened by the passage of gallstones."

Diagnosis. The diagnosis of acute pancreatitis is the most important question that confronts us. Even a cursory examina-

[1] Verhand. Deut. Ges. f. Chir., 1906, xxxv, 280.
[2] Arb. aus d. chir. Klin. d. K. Univ., Berlin, 1906.
[3] Quoted by Doberauer, Arch. f. Phys., 1904, p. 334.
[4] Trans. Assoc. Amer. Phys., 1908, xxiii, 540.
[5] Jour. Med. Research, 1907.

tion of recorded cases will show that in 90 per cent. the correct diagnosis has not been made, except at operation or autopsy. Indeed, even at operation the condition has been overlooked in not a few instances (as in a case lately reported as one of a series by Noetzel[1]).

The symptomatology, therefore, must first be considered. Fitz[2] gives us the best concise statement of the classical symptoms: "Acute pancreatitis is to be suspected when a previously healthy person, or sufferer from occasional attacks of indigestion, is suddenly seized with violent pain in the epigastrium, followed by vomiting and collapse, and in the course of twenty-four hours, by a circumscribed epigastric swelling, tympanitic or resistant, with slight rise of temperature."

The pain, as a rule, is severe, and generally referred to the epigastric region. It was so in all of my cases (II, III, V, VI) in which this is recorded. It has been asserted by some that it is more often to the left of the median line, and while this may be a point of some value when it is present, the absence of localization of the pain to the left side should not influence us in the least in estimating the importance of this symptom. The existence of severe epigastric pain was noted in several cases reported by Mayo Robson, in the two reported by Bornhaupt,[3] in a case reported to me in a personal communication by Dr. Chase, of Philadelphia, and in several of those reported by Doberauer and Noetzel, and those of Murray[4] and Bell.[5] On the other hand, in several of the cases reported by Doberauer, the pain was referred to in a more general way as being abdominal. Indeed, in one case operated by Noetzel, the patient spoke of the pain being in the lower abdomen to such an extent that the operator made his first incision for a supposed pelvic condition.

There is never any doubt concerning the severity of the pain wherever located. It practically always calls for the guarded

[1] Beitr. z. klin. Chir., 1908, lxxv, 735.
[2] Quoted by Robson and Cammidge, Diseases of Pancreas, 1908.
[3] Deut. med. Woch., 1908, xxxiv, 1306.
[4] Trans. Amer. Surg. Assoc., 1902, xx, 219.
[5] Ibid., 1904, xxii, 103.

use of opiates, although these are often without avail. This was true in Case VI of my series, in which the pain was agonizing and but little affected by several hypodermic injections of morphine. Associated with the pain, but a far less constant symptom, is epigastric tenderness. In many cases it is but slightly marked, although careful examination will usually elicit it. It becomes more marked if the case progresses to suppuration, especially with the formation of a mass, which is practically always tender. In the same way epigastric muscular spasticity may occur as the result of the local condition.

Soon after the onset of the pain there is vomiting—a practically constant symptom. The vomiting, in some instances, lasts but a few hours or perhaps a day—as in Case V; and in others it becomes almost uncontrollable and progressively worse. This is a diagnostic sign of but little value, as it is common to most acute intra-abdominal conditions. Attention has also been called to the fact that it is, as a rule, biliary in character. Indeed, vomiting, especially when persistent, is one of the most misleading symptoms of the disease under consideration, as it often serves to make a diagnosis of intestinal obstruction seem the correct one. I have, however, never noticed fecal vomiting, which is always present in the late stages of intestinal obstruction.

Persistent and uncontrollable belching and hiccoughing are marked symptoms of acute pancreatitis. They are often sufficiently severe to draw the physician's attention to the possibility of some trouble near the diaphragm, and to help to a correct diagnosis. They were especially noted in Case VI of my series, and were far more troublesome than the vomiting itself.

Collapse in the acute onset of pancreatitis is often very marked. In some of the cases, operated and unoperated upon, it may pass very quickly on to a fatal termination. In others, the patient recovers from it sufficiently to last for a few days, in very rapid cases, or even recovers therefrom entirely when a localized pancreatic suppuration supervenes. Fitz and others have called attention to the marked cyanosis which occasionally accompanies this collapse, and it has been referred to as a diagnostic feature.

Its cause is still unexplained. It was not noted in any of my cases, but was a feature in the case personally reported to me by Dr. Chase.

A possibly important symptom in the onset of acute pancreatitis is the frequent presence of a slow pulse even during the collapse, and until a septic condition supervenes. Indeed, it may even persist under these circumstances. I have had several instances of this fact sufficient to convince me of its *occasional* significance. Thus in Case II the pulse was never very rapid, and dropped even to below 100 when the other symptoms abated. In Case III, an ultra-acute one, the pulse on admission was 76. References to the suppurative and less acute cases, Nos. IV and V, show a comparatively low pulse rate. In Case VI, during the primary agonizing pain and collapse, the pulse was about 80 to 90 per minute, even when the temperature dropped below 96° F. In this instance, however, the pulse became very rapid and feeble as soon as the marked pancreatic toxemia had a chance to manifest itself.

So far I have been discussing practically only the symptoms immediately associated with the very onset of the disease. If the patient survives the initial shock or hemorrhages, as the case may be, certain other conditions make themselves manifest. There are evidences of intestinal paresis. Besides the vomiting and belching already spoken of, there is frequently, in the first two or three days, interference with the passage of gas and feces. After several days repeated enemas will usually give quite copious and bulky stools. Associated with these conditions there is intestinal and abdominal distention, with corresponding distress. Very often this seems to be largely colonic, affecting principally the transverse and descending colon, the small intestine being involved to a lesser extent.

Slight jaundice, as noted in Case VI for forty-eight hours, and in Case II and Case V (with cholelithiasis) is of frequent occurrence in pancreatitis. As a diagnostic sign it would serve only the purpose of calling our attention to some lesion in the upper abdomen.

The formation of a more or less well-defined epigastric mass, apparently deep, usually somewhat tender, and often to the left of the median line, is very suggestive of pancreatitis, when found in conjunction with some of the other significant symptoms. Formerly, when cases were kept under observation longer, because of failure to diagnosticate them and reluctance to operate, except in the face of very definite indications, this was more often seen than it is now, when the tendency is to operate somewhat earlier. Case VI showed this feature most markedly, that is, the presence of a deep indefinite resistant area in the left epigastrium. Some suggestion of it was noted in Case IV. In the case reported to me by Dr. Chase this feature was most marked.

Naturally the presence of a tumor, such as this, can hardly be expected in those instances of acute pancreatitis which quickly terminate fatally. The swollen, engorged, or hemorrhagic pancreas itself is hardly ever palpable. The hemorrhage in and about the pancreas itself scarcely ever gives us such a considerable mass that palpation is possible, yet even this must be considered within the range of possibility.

Finally, there is to be mentioned that occasional occurrence of dulness or of impaired resonance and breath sounds over the lower lobe of either lung, usually the left. This occurred in Case VI of my series, and led to a diagnosis of pleurisy as a complication. The condition was present at the time of operation, but then was not interferred with. I believe it was due to infection through the diaphragm.

While the diagnostic points in acute pancreatitis are not uniform, there are enough, in at least a certain percentage of cases, to enable us to diagnosticate the condition.

Differential Diagnosis. The differential diagnosis is a matter of some difficulty in most cases. In the majority of instances in which an incorrect diagnosis has been made, it has been that of acute intestinal obstruction. It is not difficult to see why this is so. In both conditions we have the sudden onset, the violent, cramp-like pain, a slow pulse in the beginning, some distention which gradually increases, and vomiting following

the pain, with stoppage of gas and feces. The similarity is heightened by the fact that in pancreatitis the distention is largely colonic, and this often leads to a suspicion of an obstruction low down. At the onset of the disease it may be impossible to differentiate the conditions, yet the uncertainty should not last very long. In the first place, it is rare to find shock, with occasional slow pulse and cyanosis, in intestinal obstruction. The pain rather, where extremely severe, causes the patient to look blanched and exhausted. Moreover, it is, as a rule, localized to some point in the lower abdomen, rather than in the epigastrium, as in pancreatitis. Yet, as I have mentioned in discussing the symptom of pain, atypical locations thereof in pancreatitis are not entirely unknown. As the case progresses for some hours the distinction becomes slightly plainer. The vomiting in obstruction is one of the cardinal symptoms. It is persistent, severe, and becomes progressively worse. The vomitus becomes foul in a short time. In pancreatitis the vomiting is bilious in practically every instance; after a short time it becomes less frequent. Far more distressing is the hiccoughing and belching associated with pain. These seem to be much dwelt upon in the case histories of pancreatitis, and were illustrated to a marked degree in Case VI of my series. They are not so prominent or striking in cases of obstruction. In pancreatitis the distention is generally colonic and not of high grade. In obstruction it may or may not be localized to the colon, is more marked and more quickly progressive. In pancreatitis the ileus may be absolute at first, yet often high enemas result in passage of gas and true bowel movements. In acute obstruction we can, by the same means, obtain only emptying of the lower part of the larger bowel, and the passage of flatus, if it occurs at all, is very limited.

In pancreatitis the development of epigastric pain occurs frequently and often early, while in obstruction we have practically never a localization of these signs to the epigastrium. Slight jaundice often develops in pancreatitis; in obstruction it is absent. The rapid development of free fluid in the abdominal cavity would point to pancreatitis. If the case should progress for some days,

we have in pancreatitis the gradual appearance of signs of omental bursitis, an upper abdominal lesion, associated with a severe toxemia, but with subsidence of the signs of ileus, vomiting, etc. In obstruction there is also a toxemia from the absorption of stagnated bowel contents, and the signs of intestinal stasis plainly manifest themselves if continued; finally, there are fecal vomiting, increasing signs of peritonism, marked distention, and tympany.

The mistake of diagnosticating a case of acute pancreatitis as obstruction was made in Case III. With the increased understanding of the subject which we now have, and perhaps a slightly more extended study of the case (which was operated upon at once on admission), the diagnosis, I believe, could perhaps have been properly made. It is a most noticeable feature of all the more extended series of cases of pancreatitis reported, that in the earlier ones the diagnosis was but rarely made, while in the later ones seen by any one man it was practically always strongly suspected, if not definitely decided upon.

Acute gastroduodenitis has been mentioned as possibly to be confused with pancreatitis. It must, indeed, be a severe type of this illness which would simulate the graver lesion. Indeed, it seems hardly more than necessary to consider the symptoms of each to arrive at a diagnosis, should this be the differential question.

Biliary colic, with or without slight jaundice, would give us many points of similarity to the initial pain of pancreatitis. At the time of the onset of the pain a distinction might be impossible. Gallstone colic is far more common than acute pancreatic lesions are, and they may be associated, as in Case V, so that the physician would think of that condition first. As a rule, the location of the pain to the right of the median line, its radiation, and the failure of other pancreatic symptoms to supervene should guide us correctly. Yet it is to be remembered that in pancreatitis the location of the pain is variable, and radiation to the back and shoulders has been mentioned as at times occurring.

The diagnosis would be more difficult when we have a perforative peritonitis as the result of some lesion in the biliary passages.

This condition would more closely resemble other varieties of perforative peritonitis of the upper abdomen, and will be grouped with these in the discussion thereof.

Other conditions referred to as possibly simulating acute pancreatitis have been poisoning, impacted ureteral calculus, etc. In these the course of events, the other and distinctive signs, and in the former the history, should soon serve to put us on the right track.

Thrombosis of the mesenteric vessels, practically never diagnosticated except at operation, may give us symptoms of ileus and peritonism, very likely to simulate acute pancreatitis.

Acute appendicitis has been the diagnosis of several cases of pancreatitis. It does not seem to me that these conditions are sufficiently similar to cause the mistake to be made often. Appendicitis is distinctly an inflammatory condition of the lower abdomen; its symptomatology is well marked and typical in most cases, and its signs, with few exceptions, are not those of an upper abdominal lesion.

Next to a diagnosis of acute obstruction in those cases of pancreatitis not recognized, there is that of an acute perforative peritonitis of the upper abdomen, be it of stomach, duodenum, or bile ducts. In the first two conditions we can generally get a history which would be something of a guide to us. When the biliary system is the seat of perforation, the history may be misleading rather than a guide to us. In all these conditions the sudden agonizing pain in the epigastrium would at once point to a serious lesion of the upper abdomen.

Treatment. The treatment of acute pancreatitis is one of the most important subjects which confronts the surgeon. The comparative rarity of the condition, the different phases it may assume, and the varying degrees of its severity make the treatment of first importance.

But a few years ago pancreatitis, except when progressing to suppuration, or the formation of a palpable mass, was considered to belong to the field of medical treatment alone. Surgical intervention was considered hazardous and almost useless. Several

cases have been reported as recovering without operation, in which there were apparently the symptoms of an acute pancreatic lesion. I have seen this occur in acute pancreatitis and in acute exacerbation of chronic pancreatitis. Needless to say, recovery under these circumstances, is rare; indeed, it may truthfully be stated that the chance of such a non-operative recovery is comparatively slight.

The medical treatment of acute pancreatitis has been aptly compared to a similar procedure in acute appendicitis. The latter affection was beyond the range of surgery many years after its pathology was well known. It may be admitted then that the treatment of an acute pancreatitis is by surgery only. This being so, there are three important features to be considered as regards operation:

1. At what stage of the illness shall we operate?

2. What method of approach to the seat of disease shall be adopted?

3. The technique after reaching the pancreas or the pancreatic abscess.

1. *The stage at which operation should be undertaken* in acute pancreatitis varies with the variety of the disease. In a fulminating ultra-acute case, the rapid progress of the patient from bad to worse may make early operation necessary. Operation should not be undertaken in the state of primary shock, following the onset of the distinctive symptoms of pancreatitis. Cases in which this has been done have almost invariably come to a fatal termination. The tendency among surgeons who have investigated the question, and have had the opportunity of seeing a number of cases, seems to be to operate comparatively early.

Nevertheless, I am convinced that this rule does not always hold good. Thus, in Case VI, which terminated as a gangrenous pancreatitis, with sloughing of almost the whole organ, it is almost certain that surgical intervention in the first few days would have ended in the patient's death. Our delay, with stimulation, allowed us to operate upon a patient in somewhat improved condition, and to make use of localizing signs to approach the pancreas by a

much more favorable route than it would have been possible to adopt had immediate operation been undertaken. It must be understood, then, that while in cases becoming rapidly and progressively worse operation may be imperative, it is generally of advantage to give the organism an opportunity to prepare itself, so to speak, for a still greater tax upon it. Moreover, when we delay until an abscess extending into the loin has formed, we are able to approach it through the loin. Had operation been deferred in Case III, the result could not have been more unfortunate. The formation of a mass in the upper abdomen, or the occurrence of dulness and tenderness toward the flank, would not only make our diagnosis more certain, but give us a safer route by which to approach the diseased area than through the peritoneum.

2. *The Method of Approach to the Seat of Disease.* The routes to the pancreas may be grouped under two main heads: (1) Those which involve the traversing of the general peritoneal cavity, and (2) the extraperitoneal route by the loin incision.

1. When there is a beginning acute pancreatitis, when the localizing symptoms are all epigastric, when there is a tumor palpable anteriorly, giving a tympanitic note on percussion and a sense of resiliency on palpation, and when there is doubt concerning the diagnosis, we are compelled to make our incision upon the anterior aspect of the abdomen, and to traverse the general peritoneal cavity in order to finally reach the pancreas. Once in the general peritoneal cavity, we may approach the pancreas itself either (*a*) through the lesser omentum, (*b*) through the gastrocolic omentum, or (*c*) through the transverse mesocolon. As a general rule, the anterior or intraperitoneal incision, if I may so call it, has been adopted by almost all operators. It has one serious disadvantage, that is, the risk of infecting the general peritoneal cavity. Its advantages are the free exposure of the operative field, opportunity for radical surgery, and the opportunities which it offers for the establishment of adequate drainage. The choice of a path above or below the stomach must depend upon circumstances. When we wish to secure an extra path for drainage, tampons and drains must be carried both above and below the stomach.

2. The extraperitoneal route, practically, as for exposure of the kidney, allows us to approach the pancreas, and especially the tail thereof, without entering the general peritoneal cavity. The chief advantages of the extraperitoneal route when feasible cannot be questioned, except possibly by a few enthusiasts who, by preference, open appendiceal abscesses and remove ureteral stones through the peritoneal cavity. Naturally it is only applicable in those instances in which we have a distinct indication for it, that is, the appearance of symptoms pointing to the localization of inflammatory exudate or pus in the loin. By it we get good drainage for the pancreas and the omental bursa. Its disadvantages are, however, many. We get no free exposure of the parts and radical surgery is impossible. We can drain, that is all. Gallstones or concomitant gastric lesions, etc., are entirely inaccessible by this method. Cases III and IV of my series were operated upon by the anterior incision, and correctly so as in each case the localizing symptoms demanded the opening of the greater peritoneal cavity. In Case V, after the operation for gallstones had been carried out, the postpancreatic collection was evacuated by the loin. Thus there was avoided the danger of peritonitis, and at the same time the underlying biliary condition was adequately dealt with.

In this connection I may mention the fact that in some of the reported instances of acute gangrenous or suppurative pancreatitis, drainage has been instituted by both the anterior and posterior routes. In Case VI we had an omental bursitis with distinct localizing signs in the left loin. Here it was deemed better to undertake the unmistakably less serious extraperitoneal operation, rather than to ignore the symptom which clearly indicated our correct avenue of approach to the seat of the lesion. I do not believe that we should have achieved an equally favorable outcome by any other operative procedure. The wound drained freely, the pancreas, as it sloughed, was discharged without difficulty, and our only unsatisfactory feature was the impossibility of obtaining a full exposure of the wound when dressing it.

3. *The Technique after Reaching the Pancreas.* Whether we have to deal with a pancreatitis still in the presuppurative or hemorrhagic stage, or whether pus has already formed, we have but one cardinal indication for treatment—the establishment of adequate drainage.

Should we find an acute hemorrhagic pancreatitis, or an acute gangrenous pancreatitis, having approached the organ by the intraperitoneal route, our only possible procedure locally is to apply tampons and drains freely to the organ itself, going either above or below the stomach. I believe that tube drainage is always essential. Gauze alone will do more to prevent than to establish drainage.

In a previous article I have stated it as my belief that when we find an engorged and inflamed pancreas it is expedient to incise the capsule and to apply our drains to this exposed surface. I have since then had no further experience with a case requiring this treatment. Certain recent investigators, however, have come to the conclusion that this incision into the organ itself is unnecessary. Noetzel, especially, who has written the most recent resume on the subject takes this stand. He brings strong support for his argument from his own experience and that of others. In the present state of our knowledge it must be admitted that the question is still open.

It is practically never possible satisfactorily to resect the pancreas for inflammatory lesions, and this is, indeed, unnecessary. Drainage gives free exit to the debris.

Should there be any free fluid in the peritoneal cavity it will be necessary to see to its removal. It should not be forgotten that in this pancreatic exudate we have toxic material often sufficient to cause death. In this connection it is interesting to note that in one of the first cases of this kind reported, that of Halsted, the evacuation of the free fluid in the peritoneal cavity was the only thing attempted. The patient recovered, and while it may be true, as Körte has remarked concerning this case, that the patient recovered in spite of and not because of the operation, yet it is doubtful if recovery would have taken place with any added toxins for him to overcome.

The peritoneal fluid may gravitate toward the pelvis. In several cases in which this was marked, tube drainage of the pelvic cavity, with the semi-erect position of the patient, has been successfully adopted.

It is almost unnecessary to mention the fact that gauze drainage in all these cases under discussion must be supplemented by the use of tube drains, preferably rubber ones of large caliber. Drainage by gauze tampons alone often defeats its own object, the saturated gauze acting only as a plug and not as an outlet.

When there is a pancreatic abscess, or an omental bursitis and peripancreatitis, free drainage either by the anterior or the posterior route is the prime essential. When pus is present it is of still more importance than under any other circumstances to use free drainage by tubes, and not to rely on tampons alone.

Some question has arisen as to the treatment of an accompanying cholelithiasis found at the time of an operation for acute pancreatitis. I believe that when the patient's condition warrants it, we should correct also the underlying and really primary biliary condition, and so avoid any probability of again having to perform a serious laparotomy. Often, as Noetzel has pointed out, the gravity of the pancreatic condition and the weakness of the patient will prevent us from thus completing our operation. And in several reported cases, such as that of Stieda, the leaving of biliary calculi has apparently been no hindrance to the complete recovery of the patient from the pancreatic condition. If there is any doubt in the operator's mind as to the advisability of dealing with the accompanying cholelithiasis, he had better defer. Two operations and recovery are preferable to one operative procedure with a fatality.

The preparatory treatment for operation must evidently be very brief in most cases of acute pancreatitis. It does not offer us great possibilities. We can do little to help the patient to stand the shock of surgical intervention beyond the use of the ordinary stimulants, etc. Speed and the avoidance of shock and chilling on the table play a far more important role in helping the patient to ultimate recovery.

Postoperative treatment is the same as in all other serious laparotomy cases, with but few added features. Drainage should be left in until it has very evidently fulfilled its functions—until there is nothing more to drain.

Recently, Wohlgemuth[1] has, by experiment and also clinically, shown that by placing patients who have been operated upon for pancreatitis upon a typical antidiabetic diet we can so alter the pancreatic secretion that it becomes less active and irritating. This fact seems to be abundantly confirmed by other observers. Not only this, but by the same use of diet, the healing of both recent and old pancreatic fistulæ is accelerated. The results in this direction have been truly remarkable. This is, perhaps, the only postoperative treatment that differs in any way from that of the other suppurating intra-abdominal lesions and abdominal sinuses.

DISCUSSION.

Dr. David Riesman: In a case of acute pancreatitis that I saw some years ago I noted a severe persistent dyspnea which was not accounted for by anything in the heart or in the lungs. I should like to ask whether Dr. Deaver or anyone else has noticed this symptom. The possibility that a diaphragmatic pleurisy might give rise to the clinical picture of acute pancreatitis seemed to be proved in a case I recently had under observation. The symptoms in the beginning were entirely abdominal. When I saw the patient (a married woman, aged thirty years) several days later the abdominal symptoms had subsided and a pleural effusion was demonstrable. Eventually nearly a quart of blood-tinged fluid was removed by tapping. A moderate reaccumulation occurred, which, however, was absorbed, the patient making a satisfactory recovery. I cannot conceive this case to have been one of pancreatitis, but believe that it belongs to the fairly common group of pleural and pulmonary diseases with inaugural symptoms in the abdomen.

Dr. Joseph Sailer: I regard the paper by Dr. Deaver as the best one written upon pancreatitis up to the present time. Compared with the articles on pancreatitis in the best text-books, such as that of Robson and Cammidge, it is markedly superior. From my standpoint the section on diagnosis is admirable and more complete than any I have read. I am sorry that Dr. Deaver did not quote the work of Dr. Williams, which shows conclusively that acute pancreatitis can be produced experimentally under aseptic con-

[1] Berl. klin. Woch., 1907 and 1908.

ditions. It has also been shown by Claude Bernard that experimental acute pancreatitis can be produced and made to run a fatal course in such a brief period of time that bacteriological infections are practically excluded. I do not mean that Claude Bernard excluded bacteria, for he was not aware of their significance, but experimentally he showed that death might occur in a few hours. At the Pepper Laboratory Dr. Speese and I were able to cause death in dogs by injecting oil into the pancreatic duct and then ligating the duct in about eight hours.

In the majority of cases, as Dr. Deaver has suggested, the infection is usually secondary when there are pathogenic organisms; although it frequently occurs that pathogenic organisms may cause a lesion which in turn causes acute pancreatitis, and then subsequently, if the patient survives long enough, an infectious pancreatitis may occur. Guleke and von Bergman have surmised that the cause of the symptoms in acute pancreatitis is the trypsin intoxication. It does not seem to me that their method is absolutely conclusive. Dogs were immunized to trypsin and then acute pancreatitis produced in the usual manner. The pathological lesions were the same as in the controls but the clinical symptoms very mild. They succeeded in immunizing very few dogs. A certain number of animals are always likely to recover and go on into a state of chronic pancreatitis.

Dr. Deaver did not mention the Cammidge reaction. In acute pancreatitis, if you wait for the Cammidge reaction you will probably jeopardize the life of the patient whether the reaction be absolutely diagnostic or not. It seems to me that the Cammidge reaction must occur in other conditions than acute pancreatitis, and might be misleading.

It is a curious thing that in calculi of the pancreas, which I have an idea are not as rare as we suppose at the present day, acute pancreatitis very rarely occurs. Chronic pancreatitis is almost the rule in these cases, but I really cannot recall at this moment any case of acute pancreatitis in which calculi of the pancreatic ducts were the exciting cause of the lesion. In chronic pancreatitis it seems as if we had a definite medical treatment. I have seen two cases of the condition; one in which there were apparently calculi in the pancreas with colic referred to a point just above the umbilicus. In this case the possibility of renal calculus was suggested. There was Cammidge reaction with remarkable inability to digest carbohydrates. Extract of pancreas in glutoid capsules was given.

Dr. D. L. Edsall: As a matter of interest in relation to the ultimate results of surgical treatment of acute pancreatitis, I would mention a case which I saw in conjunction with Dr. Jurist about a year after operation by Dr. Deaver. This was a very severe case of acute pancreatitis, in which large fragments of the pancreas had sloughed away. I had the opportunity of studying the man in careful detail, and found him in good general nutrition,

showing absolutely no signs of his illness except that he was slightly under weight. He was entirely free from any glycosuria, even when fed freely on starches and sugar. His digestion appeared to be entirely normal. The ordinary gross and microscopic examination of his stools showed nothing abnormal; an accurate study of the absorption of nitrogen and fat showed no evidence of disturbance of digestion or absorption. It is true, to be sure, that various experimenters insist that even tying off the ducts of the pancreas does not interfere in many cases with nitrogen or fat absorption, but such statements appear to have been shown to be incorrect through the recent work of Pratt, and to have been due to errors in technique, especially to imperfect tying of the ducts, so that I think we may still consider that complete loss of pancreatic function is, so far as we know, associated with decided disturbance with the absorption of fat and nitrogen. The man whom I have referred to must have had extremely extensive destruction of the pancreas and yet the part remaining must be functionating satisfactorily because of the entirely satisfactory absorption and other conditions. This is not surprising, because we do clearly know from the work of Minkowski, and others since his time, that in relation to diabetes small portions of the pancreas are entirely sufficient to carry on the functions of the organs under ordinary circumstances, a fact which is merely another instance of the general fact that most of our functions are, as Dr. Meltzer has insisted, provided for us in superabundance, and we can stand the loss of a large proportion of the share that we have of most things without suffering in health as a consequence, at least so long as we are not under any especial degree of strain.

Dr. John H. Musser: It is of great interest to note regarding the work of Dr. Fitz that, notwithstanding the work was published twenty years ago, very little has been added to our knowledge of the clinical course of the disease of acute and chronic pancreatitis. What factors have been added have been those in relation to fat necrosis on the one hand and perhaps the occurrence of leukocytosis. I would lay greater stress upon some features in the previous history of the case as suggestive of pancreatic disease than apparently Dr. Deaver has, in that I should say that in cases of previous attacks of cholelithiasis or cholecystitis, pancreatic disease is more likely to follow; or, that pancreatic disease is very frequently preceded by attacks of cholelithiasis or cholecystitis. In ten or more cases this was a very prominent feature of the previous history of the cases. Then in a large proportion of cases one sees the type of individual that we see in cholelithiasis, the fat subject who has not taken much exercise, and for the same reason, apparently, that there is gall-bladder infection, there is likelihood of pancreatic trouble. We must remember that trauma, as pointed out by Fitz, is a cause of acute pancreatitis.

The clinical course is significant, for while the general phenomena are of the fulminating type, yet the temperature is lower than one would expect

in such an infection as is indicated by the severe abdominal symptoms. The temperature is usually 100°, or 100.5°, or 101°. Rarely do we see it very high. There follows the phenomenon of a tumor behind the stomach, and in a demonstration of the physical signs of the disease in the early periods one must attempt to make that out, while signs of pleuritis of the left base and later the signs of fluid in the lesser peritoneal cavity are present.

I call attention to the occurrence of leukocytosis in almost all the cases, and it is certainly more frequent in my experience than the occurrence of the same thing in intestinal obstruction, a point which we can rely upon in the diagnosis.

Of course, the great difficulty in diagnosis is to distinguish between infection of the gall-bladder and infection of the pancreas, and in some instances, perhaps the large majority, it cannot be done. Only recently I had a case operated upon in which there were well-defined attacks of biliary calculus at intervals with jaundice for six months previous to this operation. There was moderate fever, localized tenderness, and the phenomenon of infection in the upper abdominal cavity. Leukocytosis was marked, and I felt that we had to deal with infection of the biliary passage. There was found, however, an acute pancreatitis which was drained from the front and the patient got perfectly well. The hemorrhage, however, was recent and there was no indication of old hemorrhage. At first there is some resistance over the upper left quadrant. Later this becomes more or less general and one would think it due to peritonitis. But in the two or three instances in which it became general and in one instance in which it was most extraordinary we found it due apparently to the origin of the foci of fat necrosis underneath the peritoneum and with no indication of peritonitis present. The occurrence of fat necrosis one could see in the omentum and subperitoneum and might give rise to such phenomena.

Dr. Alfred Hand: After listening to Dr. Deaver's paper and the discussion I feel a little better than formerly when recalling a case in which I did not make a correct diagnosis. There were some unusual features in the case which misled me from the start. The patient, a clergyman, was sent to the hospital with the diagnosis of appendicitis, but the surgeon could find no trouble with the appendix and referred him to me. My diagnosis was typhoid fever, with the probability of some surgical complication. The temperature continued elevated—102° to 103°, and sometimes 104°, never coming down to 101°. The spleen and liver were both enlarged. He complained of abdominal pain, and that which we learned too late was that the pain was at first epigastric and deep-seated. There was a constant leukocytosis, to which, as I now look back, I feel I should have attached more importance. The Widal test was repeatedly negative. I blame myself for not having paid more attention to that, but I explained this by thinking that the reaction was

delayed. For the first five days the stomach was very irritable. There was almost constant vomiting, and the bowels were moved three and four times a day. After four or five days the stomach apparently settled itself, and for five days more liquid nourishment was taken and retained. Then, in a sudden vomiting spell, a large amount of chocolate-colored fluid was brought up, and the patient went into collapse and died in a few hours. Autopsy showed areas of fat necrosis, and the head of the pancreas was found disintegrated. There was chocolate-colored fluid in the lesser peritoneal cavity and in addition two large abscesses of creamy pus behind the splenic and hepatic flexure of the colon. Gallstones were not found.

Dr. Richard C. Norris: I do not know whether there can be any relation between the child-bearing process and the rapidly fatal form of acute hemorrhagic pancreatitis. The case I would report died on the fourteenth day of her puerperal period, having prior to that time had a perfectly normal convalescence. She had had a visit from her husband in the afternoon, and expected to return to her home the next day. She had had no bad symptoms whatever. At seven o'clock in the evening she suddenly vomited and complained of epigastric pain. I saw her at that time. Her pulse and temperature were normal. She complained of very violent epigastric pain, was much distended, and her bowels had not moved during twenty-four hours. She rapidly became worse, vomiting became incessant, the bowels could not be made to move by the most active measures, and her pulse became more and more rapid. I opened her between two and three o'clock the following morning in a condition of profound shock, expecting to find acute obstruction or a perforated viscus. She never rallied from the operation of irrigation and drainage, and died the next morning. Dr. Lavenson made an autopsy and found acute pancreatitis of the hemorrhagic variety. I should like to ask Dr. Deaver as to the propriety of immediate surgical operation in this acute hemorrhagic variety which fells an individual as if stricken with a club. The woman was in perfect health apparently, and within a few hours passed into an alarming condition which rapidly became fatal. It seems to me that these fulminating cases should not be operated upon during this first stage of overwhelming shock and collapse.

The autopsy of this case disclosed no lesion of the gall-bladder or ducts. She was an elderly primipara—forty-four years of age and had had a hard but natural labor. Whether her tremendous expulsive pains had forced into the pancreas through its duct a ferment foreign to that organ and hemorrhage followed the necrotic action of that ferment on the bloodvessels of the pancreas I cannot say. I believe pathologists recognize that as a possible source of hemorrrhage in these cases, and if that be true the relation of this accident to labor assumes an importance heretofore not recognized.

Dr. J. C. Wilson: I have seen a number of cases of acute pancreatitis, and saw one of the cases reported by Dr. Deaver. While in most of the cases a positive diagnosis cannot be made, there is a group of cases in which such a diagnosis can be made with reasonable assurance. Those are the cases in which the attack is fulminating with collapse symptoms, tension and deep-seated pain in the epigastrium, while the lower part of the abdomen remains more or less relaxed without much tenderness upon pressure and without violent spontaneous pain. The cases in which this symptom complex has occurred have given a history of cholecystitis and cholelithiasis. In three instances there had been habitual alcoholic excesses.

Dr. Sailer's remarks on the delay incident to the Cammidge reaction are very pertinent. It is important not to postpone surgical intervention in order to make a diagnosis by ordinary methods. It seems to me that this group of cases illustrates some remarks made by Dr. Roberts several months ago, to the effect that the occurrence of sudden collapse symptoms in an individual who had been in previous good health or who has suffered from cholelithiasis demands immediate surgical intervention, and that any delay incident to efforts to determine by non-surgical methods the exact nature of the lesion should be avoided.

Dr. Deaver, closing: In answer to Dr. Sailer, I would say that the work of Dr. Williams and his colleagues is noted in the paper, but to save time this part was not read. The experimental work is of interest and of great moment, but the work of this paper referred to the practical side in connection with the human subject. Regarding the Cammidge reaction, I agree with Dr. Sailer too. In my hands at the German Hospital it has not been particularly satisfactory. I believe that the majority of cases of acute pancreatitis have had a chronic pancreatitis just as the majority of cases of acute appendicitis have had chronic appendicitis. That medical treatment is of no value in chronic pancreatitis is clear. Surgery in chronic pancreatitis promises much. Anything short of that is taking advantage of your patient's confidence. Dr. Edsall referred to the case in which portions of the pancreas ulcerated. The entire pancreas except the head separated. With Dr. Musser I agree that little has been added to our knowledge of acute pancreatitis since the work of Fitz. Mayo Robson deserves all credit for the work concerning chronic pancreatitis today and not Fitz.

In regard to previous attacks of cholecystitis, I agree with Dr. Musser that the gall-bladder holds close relation to the pancreas. We have chronic disease, and then acute disease supervenes.

I agree with Dr. Musser also that infection without doubt is through the various lymphatics. Infection can go from below upward. I do not agree with Dr. Musser regarding trauma as an etiological factor in pancreatitis.

Resistance over the region of the pancreas was spoken of. This is true, but the resistance is not so characteristic here as in some other conditions.

Dr. Riesman spoke of diagnosis. I have noticed dyspnea, but I think it is due to encroachment on the diaphragm.

Dr. Hand's case was interesting, but it unfortunately died. Dr. Norris' patient also died. As to the propriety of operating upon cases of this kind, I believe it is not the best thing to do, and that if I had acute pancreatitis, I would take my chances by waiting a day or two at least, if not longer.

CONGENITAL SINGLE KIDNEY; PRACTICAL SIGNIFICANCE OF THE CONDITION, WITH STATISTICS.*

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THE subject of "single kidney" is admittedly of considerable surgical and anatomical importance, but it is also one of decided interest to the internist and pathologist. The condition was known to and imperfectly described by some of the early writers, more particularly Vesalius and Eustachius. Various classifications of "unsymmetrical kidney" have been proposed first by Morgagni in 1769, and later by Rokitansky, Morris, and other writers. These have, as a rule, included cases in which one kidney is merely atrophied as the result of disease, or undeveloped, and also the instances due to a fusion of the two organs. I have, however, discussed here only cases in which one kidney is entirely and congenitally absent. All those instances in which any rudiments or remnants of renal structure were detectable in the situation of the kidney have been omitted from consideration.

As regards frequency of occurrence of the condition, there is a marked diversity of opinion among writers. According to MacDonald Brown,[1] cases of single kidney are exceedingly rare. For example, in nearly 12,000 autopsies made in the various London hospitals prior to 1893 only three cases were found. He continues: "Indeed, only slightly over 100 cases have been recorded altogether, and even many of these were doubtfully true 'single kidney.'"

Morris[2] observed but 2 cases in 8069 cadavers, Sangalli[3] 3 cases in 5348 necropsies, Menzies[4] 2 cases in 1790 sections, Petersen 1 case in 1500, Camargo[5] 2 cases in 3000, Owtschinniskow[6] 1

* Read December 1, 1909.

in 3800, White and Martin (quoting Mawkiewiez)[7] 1 in 3992, and Rootes[8] one instance in 600 autopsies. Ballowitz[9] prosected 617 bodies (of which 121 were females) and found one example of "single kidney" associated with defective development of the genitalia of the same side. He also observed two additional cases through the courtesy of his colleagues. Preindelsberger[10] found two instances of "single kidney" in 1344 sections, Reinfelder[11] in the Munich Pathologic Institute met with 1 case in 400 autopsies, and Winter's[12] statistics show 13 cases out of 32,415 sections. Heiner[13] (through the courtesy of Dr. Sternberg) presents the figures of the Prosector at Brunn. Out of 8853 sections from 1895 to 1905, 3 cases of asymmetric kidney were found. Again, of 2145 sections from 1906 to February, 1908, two subjects showed total absence of one kidney.

Among American authors, I find Weir[14] contending that single kidney occurs only once in 5000 subjects, and Guiteras[15] found on analyzing a table of 15,904 autopsies that in four cadavers there was absence of one kidney, *i. e.*, complete absence of one organ in about 4000 instances. Says Dennis,[16] according to available statistics, complete absence or extreme atrophy of one kidney is found once in 2650 cases. The statistics obtained from the records of routine postmortem work in certain leading hospitals of Philadelphia give somewhat similar results. For example, at the Pennsylvania Hospital 1 case was met with in 1250 post mortems; in 600 necropsies conducted at the Protestant Episcopal Hospital by Dr. Wm. Egbert Robertson, no case of the sort was encountered. Dr. C. Y. White informs me that he has not met with a single case of complete absence of one kidney in a personal experience covering 1800 autopsies. On the other hand, the records of the Philadelphia Hospital furnish 8 cases out of a total of 6240 autopsies (see table).

Moore[17] (in 1898) found in averaging certain previous statistics that the "expectation" of "unsymmetrical kidney" was about one in 2400 autopsies. The aggregate of the foregoing figures, together with those accessible among the hospitals of Philadelphia, at present writing, or a grand total of 92,690 post mortems gives a ratio of one in 1817 autopsies.

The precise number of cases of congenital single kidney recorded in literature, answering to the definition given above, remains somewhat in doubt on account of the vague character of the reports of some of the earlier writers. Ballowitz,[18] in 1895, collected from the literature 210 cases, which in addition to 3 observed by himself, gave a total of 213 cases. Moore, in 1898, published 12 additional references, and thus brought the total number up to 225 cases in that year.* The two writers last cited (like myself) aimed to exclude those instances of "unsymmetric kidney" in which the organ was much wasted as the result of disease processes, was undeveloped, and those resulting from fusion of the kidneys. Radasch,[19] in 1908, wrote: "If we accept 240 cases up to the appearance of Ballowitz's paper then at least 15 more must be added, making a total of at least 255."

The writer has endeavored to collect the cases of genuine "single kidney" to be found in the literature since the publication of Moore's article in 1898 (a considerable number having escaped the scrutiny of more recent writers), together with a few scattered earlier cases with a view to showing the grand total of all recorded instances of the condition to date.

With the kind aid of my associate, Dr. H. Leon Jameson, I have found in accessible literature and the autopsy records of certain Philadelphia Hospitals no less than 61 genuine cases, making the sum total to date 286 cases. These are reasonably accurate figures and in future the number of cases belonging to this category need not remain in doubt, since the reports will doubtless be far less ambiguous than those of the earlier writers. I consider it to be a matter of considerable importance to have secured statistics, the results of an analysis of which point to definite conclusions, both as regards the question of "expectation" and that of the pathological and practical bearings of "single kidney." A consideration of the figures given in the subjoined table, in which 61 instances of the condition are detailed, will show interesting results.

* This writer actually published thirteen references, but one was probably a horseshoe kidney, hence omitted.

Reporter	Age and sex	Which absent	Ureter	Renal artery and vein	Corresponding suprarenal	Condition of genitalia	Condition of existing kidney as to size, shape, position, and lesions present.
Darby[20]	60 yrs.; female	Left	.....	Absent	Absent	.....	Kidney healthy; carcinoma of bladder and lungs.
Isaacs[21]	3 mos.; male	Left	Absent	....	Present	.....	About twice natural size, 2¾ x 1¾ x 1¼ in.; lobulation characteristic of infantile kidney; healthy; deceased of pneumonia.
Turner[22]	Past middle life; female	Left	.....	Absent	Present	Uterus unicornus	Not hypertrophied; no lesion.
Wier[23]	Male	Left	Absent	....	.....	.....	Enlarged, 5 oz., 2 drams; normal, healthy.
Ingals[24]	Middle aged; male	Right	Lower end dwindled for 4 in.	....	.....	.....	Normal size, roughened surface, pale and hard, cortical substance thick; contained two cysts.
Fenby and Walker[25]	...	Right	.....	....	.....	.....	Enlarged, weighing 9½ oz.
Peabody[26]	21 yrs.; female	Left	Absent	Two right arteries, none on left	Present	Uterus bicornate; right side better developed	Normal situation, double normal size.
Peabody[27]	61 yrs.; male	Right	Absent	Two renal arteries to left kidney; none on right	Present; normal	Normal	Double usual size, capsule of Bowman thick; interstitial inflammation; small hemorrhagic infarction.
Church[28]	45 yrs.; female	Left	Absent	Absent	.....	.....	Very small, not larger than a large hen's egg and shaped much like one; shows interstitial nephritis.
Church[28]	65 yrs.; male	Left	.....	....	.....	.....	Very large and healthy; deceased of gastric carcinoma.
Ebstein[29]	21 yrs.; female	Right	Absent	....	.....	Right cornu of uterus absent	Chronic pyelitis and chronic interstitial nephritis.
Smith[30]	33 yrs.; male	Left	.....	....	.....	.....	Enlarged, weighing a little more than 7½ oz.
Hand[31]	...	Right	Absent	....	Present	.....	Compensatory hypertrophy; patient had lumbo-sacral meningocele.
Murray[32]	8 yrs.; male	Right	Absent	Two small vessels from bifurcation of aorta	.....	.....	Large kidney, dilated pelvis; impaction of ureter with calculus; situated in hollow of sacrum behind bladder, more to left than right.
Lohsse[33]	Adult; male	Left	Absent	....	.....	.....	Considerably hypertrophied, otherwise shows no pathological change.
Israel[34]	52 yrs.; male	Right	Absent	Artery absent	.....	Testicle 2 cm. long; is in pelvis	Enlarged, 12 cm. x 8 cm. x 6½ cm.; in normal position.
Bauer[35]	22 yrs.; male	Left	Absent	Present, but very small; vein absent	Present and normal	Left vas deferens and seminal vesicle absent	Slightly enlarged, weight 190 gms.; normal position and form.
Francois-Dainville[36]	...	Right	.....	....	.....	.....	Very large, weighing 430 gms.; surface lobulated, somewhat congested.
Beaufume and Carron[37]	47 yrs.; male	Right	Absent	....	Right absent; left weighed 9 gms.	Right testicle small but appears sound; left in inguinal canal and is markedly atrophied	Weighs 250 gms., structure unaltered; normal situation; associated with total inversion of the viscera.

Reporter	Age and sex	Which absent	Ureter	Renal artery and vein	Corresponding suprarenal	Condition of genitalia	Condition of existing kidney as to size, shape, position, and lesions present.
Guiteras[38] (Case I)	21 yrs.; male	Right	Absent	....	.....	.....	5 x 3 x 2½ in.; lobulated, had but one pelvis; showed evidence of tuberculosis and nephritis.
Guiteras[38] (Case II)	30 yrs.; male	Right	Absent	....	.....	.....	7½ x 4 x 2½ in.; not distinctly lobulated, but somewhat irregular on surface; normal position; acute parenchymatous nephritis.
Guiteras[38] (Case III)	25 yrs.; male	Left	Absent	....	Absent	.....	4 x 2½ x 2 in.; five or 6 irregular elevations on its surface; somewhat lobulated; single pelvis; chronic interstitial nephritis.
Wilson[39]	55 yrs.; female	...	Two ureters from kidney	....	.....	Some malformation of uterus	Great size; no lesions.
Crawford[40]	62 yrs.; female	Right	Absent	....	.....	.....	"Large white" kidney; cicatrix in lower pole, result of previous tumor growth (died in coma).
Nelson[41]	20 yrs.; female	Right	Present; 3¼ inches long; closed at upper end	....	Both present and enlarged, especially right	Normal	Relation of vessels normal.
Brinkman[42]	Adult; male	Left	Absent	....	Absent	Left testicle and epididymis small	Decidedly enlarged; 16.5 x 7.5 x 5.5 cm.
Winter[43]	21 yrs.; male	Left	8 cm. long; occluded above	....	Present	Normal	One large and numerous little cysts; little normal kidney structure remaining; death due to nephrectomy.
Edington[44]	2 days; male	Right	.....	Absent	Present and normal	Right vas and epididymis small	Good size, 5 x 3 x 2 cm.; normal shape, though marked lobulation; normal position shows cloudy swelling; atresia anus and harelip.
Moore[45]	35 yrs.; male	Right	Absent	Absent	Absent; left present and normal	Normal	Considerably enlarged, 285 grams; normal position.
Moore[45]	50 yrs.; male	Left	Absent; right normal	Absent; right normal	Absent; right normal	Absence of genital apparatus on left side	Much enlarged, 480 grams; marked lobulation, otherwise normal in shape; normal position; patient had diabetes and gangrene; died of pneumonia.
Mori[46]	88 yrs.; male	Left	Absent	Artery absent	.....	.....	Large, 16 x 6 cm.
Robinson[47]	...	Left	Absent	....	.....	.....	Compensatory hypertrophy, being one-third excessively developed; normal shape.
Horrand[48]	7½ mos. male	Right	Present; crossed median line and joined left before entering left ureter; was permeable	Absent	Present	Right testicle found in inguinal canal	Lobulated and hypertrophied
Viannay and Cotte[49]	60 yrs.; male	Right	Absent	Absent	Both present	Absence of right vas deferens and vesicula seminales and corresponding ejaculatory duct; right testicle small; right lobe of prostate somewhat smaller	Compensatory hypertrophy 250 gms.; normal situation.

Reporter	Age and sex	Which absent	Ureter	Renal artery and vein	Corresponding suprarenal	Condition of genitalia	Condition of existing kidney as to size, shape, position, and lesions present.
Delearde[47]	Young infant	...	.....	....	.....	.....	.....
Hollopeau[53]	50 yrs.; male	Right	Lower portion present, 13 cm. long; permeable and ends in blind pouch above	....	Present and apparently normal	.....	Normal situation; a little larger than normal.
Manson[52]	59 yrs.; male	Right	Absent	....	.....	.....	Large, weight 9 oz.; no pathological change.
Codina[48]	80 yrs.	...	.....	....	.....	.....	Abnormal form and situation; kidney showed changes of chronic nephritis.
Scheuer[54] (Case I)	3½ yrs.; female	Left	Absent	Absent	Present	Normal	Kidney showed amyloid change.
Scheuer[54] (Case II)	60 yrs.; male	Right	Present; and permeable for 1¼ cm., otherwise absent	Artery absent	Present; normal size and situation	Normal	Very much enlarged; on section, cortex found to be thickened; capsule stripped easily.
Scheuer[54] (Case III)	26 yrs.; female	Right	Absent	Absent	Present	Right ovary missing; bicornate uterus, septum extending into bladder	Enlarged, 15 cm. long; capsule adherent; numerous abscesses of kidney, ureter, and bladder.
Scheuer[54] (Case IV)	19 days	Right	Absent	....	Present	Atresia of urethra and anus	Much enlarged, partly due to hyperplasia and partly to hypertrophy.
Broek[55]	Adult; male	Right	Absent	Artery present; vein absent	Present	Absence of testicle, vas deferens and seminal vesicle; right lobe of prostate atrophied	Increased in size, 15 x 8 x 4 cm.; normal position.
Diamantis[56]	60 yrs.; male	Left	Absent	Artery absent	Present and normal	.....	160 gms.; surface smooth and regular.
Jacquin and Marquez[57]	57 yrs.; female	Right	Absent	....	Absent; left hypercystic	Lateral version	Weight 300 gms.; lobulated; normal position; evidence of chronic nephritis.
Schmidt[58]	64 yrs., male	Right	Absent	Absent	Present	Right testicle and epididymis smaller; right seminal vesicle enlarged and is seat of round and spindle-cell infiltration; no spermatozoa present	Shows enlargement, 15 x 6¼ cm.; normal situation; no histological change.
Heiner[59]	40 yrs.; male	Left	Absent	Absent	Present	Tail of epididymis, vas deferens, seminal vesicles and ejaculatory ducts missing on right side; otherwise normal	Slight increase in size due to compensatory hypertrophy; 270 gms.; normal form and situation.
McCrae[60]	49 yrs.; female	Left	Absent	....	.....	Left ovary, tube, broad ligament and left half of uterus absent	Larger; normal position.

Reporter	Age and sex	Which absent	Ureter	Renal artery and vein	Corresponding suprarenal	Condition of genitalia	Condition of existing kidney as to size, shape, position, and lesions present.
Rendue[61]	17 mos.; male	Left	Absent	....	Present; in normal position and form	Normal	Enormous compensatory hypertrophy; 6½ x 5 x 4 cm.; weight 85 gms. (normal 40–45 gms.); globular shape; no macroscopic lesions.
Orbison[62]	31 yrs.; male	Left	Could be traced upward from bladder for a few inches; enlarged	....	Present; measured 2½ x 1¼ in. and was flattened, right like left	.....	No note of vessels; kidney 7¾ x 2⅛ in.; chronic interstitial nephritis.
Mackie[63] (Case I)	9 mos.; male	Left	.....	....	.....	.....	Weighed 298 gms. and showed fatty change.
Mackie[63] (Case II)	7 mos.; male	Left	Absent	Absent	Absent	.....	Twice normal size, normal shape.
Mackie[63] (Case III)	11 yrs.; male	Left	Absent	....	.....	.....	Large, soft; shows tubercular disease.
Mackie[63] (Case IV)	34 yrs.; female	Right	Absent	Absent	Absent	Both ovaries are fibroid; small fibroid nodules in broad ligament	185 gms.; shows fœtal lobulation, is ellipsoidal; shows some fibroid and fatty change.
Mackie[63] (Case V)	53 yrs.; male	Right	Exists for most part as fibrous cord; patulous for 4 cm. from bladder	....	Normal	.....	Very much enlarged, marked lobulation; shows changes of chronic nephritis.
Mackie[63] (Case VI)	49 yrs.; male	Left	Absent	Absent	Normal	.....	11.5 x 5 x 3.5 cm.; distinct fœtal lobulations; evidence of chronic nephritis.
Mackie[63] (Case VII)	63 yrs.; male	Right	Absent	Both absent	Present; enlarged and softened	.....	Usually thick; 13.5 x 4.5 x 4.5 cm.; shows chronic interstitial change with anemic infarct.
Mackie[63] (Case VIII)	40 yrs.; female	Left	Absent	....	Present	.....	16 cm. in length; pushed upward and forward and is firmly adherent to under surface of liver and diaphragm; shows extensive chronic diffuse nephritis.
Hagner[14]	40 yrs., female	Right	Absent	Absent	Absent	.....	Kidney large, pyonephrosis.
Guthrie and Wilson[5]	30 yrs.; female	Left	Absent	....	.....	Left tube, broad ligament and ovary absent; cervix closed; hematometra; lower end of vagina absent; coitus through urethra	Diagram shows remaining kidney in normal position; size and condition not described.
Anders	64 yrs.; male	Left	Absent	Absent	Left absent; right hypertrophied	Normal	Hypertrophied; weight 240 gms.; surface lobulated, in normal situation; evidence of chronic interstitial nephritis.

Before attempting an analysis of the tabulated list of cases, however, I shall give the notes of a case personally observed, together with various conclusions to which they point:

W. B., aged sixty-four years; occupation, varnisher; native of England; weight, 160 pounds; height, 5 feet 8 inches; was admitted to the Medico-Chirurgical Hospital April 10, 1909. The family history was good, except that his father died at the age of sixty-four years of Bright's disease, and one brother at the age of sixteen suddenly, but of unknown cause.

Patient had all of the more common childhood diseases, including scarlatina; subsequently continued well until eight or nine years ago, when rheumatism developed; it was of a subacute type and did not confine the patient to bed; has had several recurrences of a similar nature during the past eight years. Last July, one year ago, while working at his trade, his right arm from elbow to finger tips particularly on the ulnar side, as well as his right leg from the knee down to the toes, manifested a sense of numbness, which, however, passed away in the course of fifteen minutes. Last July he had a similar attack, which left his hand in a drawn or partially closed condition; it is now straightened out, except that his middle finger is still distinctly contracted.

The social history is as follows: Married, three children, and up until three years ago patient was a hard drinker, using on the average about a quart of whiskey and four or five pints of beer daily; otherwise, social history is without significance.

The present illness began last October (1908), at which time he noticed shortness of breath and pains across his chest upon exertion; he was easily exhausted and complained of being constantly tired. Out of the left eye objects appeared black, and about this time he was compelled to quit work on account of weakness and a feeling of exhaustion. During the previous month, and even subsequently, he passed large quantities of urine (about one gallon per day). In March had suffocating attacks, especially at night, and went to the Johns Hopkins Hospital as a patient. Here he was told that he had kidney and heart disease, and remained about five weeks.

Physical examination revealed a middle-aged white male, conscious, rational, though with tendency to stupor, falling asleep during examination; the skin was livid, being especially cyanosed over the extremities; mucous membranes also cyanotic; marked œdema of the ankles and feet, with slight wrist drop of right arm; head and eyes normal, but nose cyanosed, and cutaneous veins engorged; no teeth in upper jaw and only a few in lower; gums showed marked pyorrhœa in lower jaw, but no blue line.

Chest emphysematous in type and respirations markedly labored. The heart's apex beat displaced outward, the impulse short and weak. The right border of cardiac dulness was about 1 cm. beyond the right sternal edge and the left 1 cm. to left of the midclavicular line. The upper border was on a level with the third rib. Auscultation revealed a feeble first sound, a soft systolic whiff at apex, with slight accentuation of second pulmonic sound (relative insufficiency). There was some abdominal distention, but no ascites. Liver and spleen were slightly engorged.

On admission the amount of urine was abnormally small, but after rest in bed, the use of saline laxatives and nitroglycerin alternated with tincture of convallaria and digitalis, the urinary secretion increased to 64 ounces, while it again decreased during the last few days of life. The pulse was rapid, and toward the close of life compressible, while the respirations ranged abnormally high, particularly during the last four days. The temperature, which had been constantly at a subnormal level until four days prior to death, also became decidedly elevated, touching $104\frac{3}{5}$ at the time of demise. The physical signs of bronchopneumonia were present during the same period. Repeated urine analyses gave the presence of a heavy ring of albumin, and numerous broad granular casts on microscopic examination; specific gravity, 1015 to 1019. The blood pressure in recumbent posture was systolic 168, and diastolic 138; during his stay in the hospital the blood pressure, however, declined considerably.

The ophthalmoscopic examination made by Dr. L. Webster Fox gave this result: Media clear, optic neuritis with marked œdema of the retina, extending back to the equator. The heads

of the optic nerves completely buried, and outlines of arteries and veins quite obscured. Striæ of hemorrhages extending completely around the optic nerve entrances; apex of the swellings at least nine to ten diopters in height. The ophthalmoscopic picture is that of a most pronounced case of albuminuric retinitis.

Patient was sleepless and decidedly breathless in paroxysms at night. Prior to the fatal termination, April 24, subcrepitant and moist bubbling rales were audible over bases of the lungs.

Autopsy made two and one-half hours after death; no rigor mortis; body still warm to the feel. Lungs œdematous; pleural adhesions both sides (no free fluid); three small areas of consolidation were found—one in left apex, another in the lower lobe of left lung, and still another in the middle lobe of the right lung. These presented the characteristic appearances observed in bronchopneumonia. Heart showed general hypertrophy, with considerable secondary dilatation (relative incompetence); weight, 515 grams; valves showed no pathological changes, except slight thickening of the mitral segments. The liver was slightly enlarged and cirrhotic; gall-bladder normal; spleen apparently normal; stomach and colon normal in size and position. Kidneys: The left kidney, renal artery, and vein, as well as ureter, were entirely absent; also the left suprarenal body and artery could not be found. The right or existing suprarenal body was somewhat hypertrophied. It was observed that the right renal artery was somewhat enlarged and bifurcated just before entering the existing kidney. The remaining kidney (Figs. 1 and 2) was present in the normal position and much enlarged, weighing 240 grams (8 ounces); it presented a somewhat lobulated appearance. Macroscopically it showed evidence of interstitial nephritis. The ureter on the right side was also slightly increased in diameter, and on tracing it downward was found to enter the bladder in the normal situation. On the opposite side no indication of ureteral orifice was noted. The pelvis of the existing kidney, while proportionately increased in size, did not show the faintest evidence of an attempt at duplication. The genitalia on the side of the absent kidney showed nothing abnormal. The prostate gland was not investigated.

Dr. E. A. Case, the pathologist, reports on the existing kidney as follows:

Macroscopically, capsule strips with some difficulty, leaving a granular surface with one retention cyst about 3 mm. in diameter. The cortex is not thinned as in typical interstitial nephritis, but as the man only had one kidney, this fact and also the massive

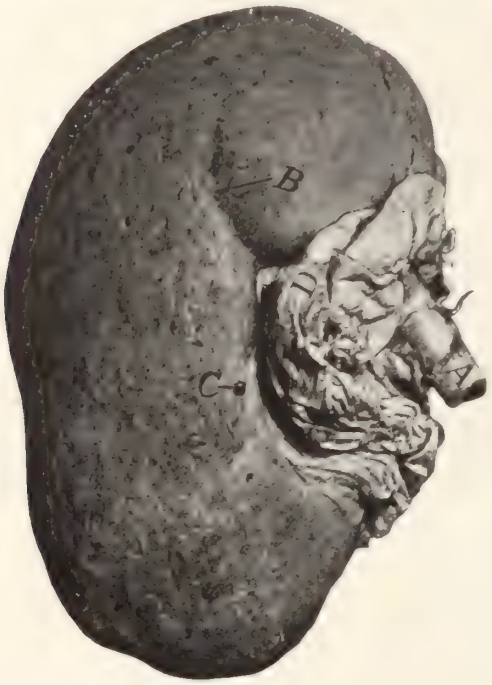

FIG. 1.—The kidney (reduced to three-fourths of its actual size). *A*, enlarged renal artery; *B*, attempt at lobulation; *C*, small retention cyst; *D*, reflected capsule.

size of the organ are probably thus explained. The cortex is only a bit irregular in thickness.

Microscopically, specimen stained with hematoxylin and eosin. The glomeruli show varying changes. Some are larger than normal, with no pathological lesion save a congestion of the capillaries of the tuft. Others are shrunken; still others converted into hyaline masses surrounded by connective tissue. In some

the Malpighian tuft has shrunken, leaving an appreciable space in Bowman's capsule. In some of the capsules of Bowman granular debris is to be seen, while others show marked thickening due to the proliferation of connective tissue about them. The convoluted tubules show parenchymatous degeneration. The epithelial cells are swollen, very granular, outline between them,

FIG. 2.—Longitudinal section of the kidney, showing a thick, somewhat irregular cortex, and absence of the section removed for microscopic study (reduced to three-fourths of actual size).

indistinct, and the nucleus stains poorly. In the lumen of the tubules there is considerable granular material. The straight collecting tubules show less parenchymatous change, and many closely approximate the normal. The interstitial connective tissue is markedly increased, being especially marked about the glomerules, but also evident about the tubules. There is also thickening of the arterial walls. In the interstitial tissue of

cortex there is an irregular round-cell infiltration composed of mononuclear cells. The bloodvessels are congested, especially in the region of the collecting tubules and pyramids of Ferrein. It is evident that the material increase in size of the kidney is due principally to a numerical increase of certain anatomical elements. The pathological diagnosis is chronic interstitial nephritis, associated with which is a parenchymatous degeneration.

While this case was not a typical example of urogenital agenesis, it was a true instance of "single kidney" or unilateral urinary aplasia, with total absence of the suprarenal capsule on the same side—a rare and interesting anomaly. It is to be noted, therefore, that it does not lend itself to the investigation of the question of the relation of "single kidney" to anomalies of the sexual organs. On the other hand, the case furnished material for a further study of the compensatory enlargement of, and of the various lesions presented by, the existing organ.

Of my own tabulated list of 61 cases, 38 were males, 16 females, and in 7 the sex was not mentioned. The right kidney was missing in 29 cases, the left in 29, and in 3 the particular side was not stated. Of the 38 males, the condition occurred on the left side in 20 and right side in 18. Of the 16 females, the left side showed renal aplasia in 8 cases and the right in 7, while in 1 the side involved was not mentioned. Ballowitz found the condition on the left side oftener than on the right in the male, the ratio being 70 to 42, while according to my figures the proportion was about even, or 20 to 18. In the female both sides are about equally affected according to my figures (vide supra).

The ureter of the side of the congenital aplasia was absent in 42, present to a greater or less extent in 9, and in the remaining 10 no mention was made. In 8 cases the genitalia were normal, in 19 abnormal, and in 34 instances their condition was not described. Of the 19 in which the genitalia showed hypoplasia, 11 were met with in the male and 7 in the female, while in one the sex was not stated. The precise character of the defects are briefly described in the above tabulated list of cases, and it will

be observed that they are remarkably variable both as to degree and nature.

The suprarenal gland could not be found in 11 instances, was present in 26, and not referred to in 24. It was missing seven times in the male and four times in the female; or in other words, in nearly even proportion in comparison to the totals for the two sexes. The renal artery was reported absent in 24 cases, present in 3, and unmentioned in 34.

The number of cases showing renal changes in the remaining organ other than mere hypertrophy was 27, those showing only hypertrophy 7, while the renal changes were not described in 27. There were 15 cases, or 55 per cent., of the total number, in which the lesions presented by the kidneys were described, that showed chronic nephritis, of which 8 were of the chronic interstitial variety. The findings in 3 cases were those of chronic parenchymatous nephritis, while 1 case presented the lesions of acute nephritis; 2 patients showed tuberculous lesions and 2 pyonephrosis; 3 had died of chronic diabetes mellitus. A single instance was furnished by each of the following conditions: Hydronephrosis, "abscessed kidney," calculus (ureteral), cystic kidney, congested kidney, amyloid kidney, and fatty kidney.

A similar consideration and analysis of all of the reported cases of solitary kidney in which the points at issue are detailed, or 286, gives us somewhat different and also more important generalizations.

Sex. In 248 cases the sex was mentioned, of which 159 were males and 89 females. As stated by Ballowitz, it is to be recollected that autopsies are less commonly made in the latter than the former sex.

Age. Of 154 cases in which the age at death was given, 34 patients were under ten years; this number, however, includes thirteen premature births. Between the tenth and fiftieth years, 62 cases occurred, and after the fiftieth year, 58 cases. Included in my series there was 1 case which had reached eighty-eight years of age and another eighty years. These figures would indicate that longevity is not markedly abridged by the occurrence of this condition.

Side. Out of 286 cases, the condition occurred on the left side in 153 and on the right side in 120, with 13 not differentiated. In 158 males the congenital urinary aplasia occurred 96 times on the left side and 62 on the right. Per contra, of 83 cases occurring in the female, the left kidney was missing in 40 and the right in 43. It would appear, therefore, that the proportions for the two sexes are diametrically opposed, but I am not in a position to offer a satisfactory explanation for the differences in sexual influence upon the side involved.

Out of the whole number, or 286 cases, the ureter was completely absent in 248. In 24 instances a more or less rudimentary ureter was in evidence without the slightest indication of the presence of renal structure.

The presence or absence of the suprarenal gland was noted in 151 cases; it was present in 109 cases and absent in 42, or 27.8 per cent. In 14 cases, the suprarenal gland on the side of the absent kidney was enlarged; in 2, it was atrophied. It is interesting to note that the suprarenal gland on the side of the existing kidney is rarely enlarged; for example, this was the case in 5 of the 61 cases included in my table, and in only 2 out of 111 cases tabulated by Ballowitz. In a single instance this organ was smaller than normal on the side of the remaining kidney. The condition of the genitalia was noted in 135 cases (out of the grand total, or 286), of which 94 showed congenital defects and 41 were obviously normal. Among the cases of genital hypoplasia were 40 males and 49 females, with 5 sexually undifferentiated.

It was found that 79 cases out of the grand total, or 170 in which the renal changes were given, or 46.5 per cent., showed morbid lesions other than mere compensatory hypertrophy. Among these 79 cases were—chronic interstitial nephritis, 19; chronic nephritis (variety not specified), 11; chronic parenchymatous nephritis, 4; acute parenchymatous nephritis, 2; ureteral calculi, 9; pelvic calculi, 6; pyelonephritis, 10; cystic kidney, 3; tuberculosis, 2; hydronephrosis, 4; "diseased" kidney, 3; stone in the bladder, 1; carcinoma of kidney, 1; "cloudy swelling," 1;

congested kidney, 1; amyloid kidney, 1; fatty kidney, 1; and abscess of kidney, 1.

Ballowitz speaks of the frequent occurrence of nephrolithiasis being emphasized by the older writers; and Mosler[65] refers to the danger to the individual attending disease processes affecting single kidney. The results of the combined statistics of Ballowitz, Moore, and the present writer indicate clearly that a greater than the normal percentage among subjects of congenital single kidney die of kidney complaints, as will be shown hereafter. Unquestionably, nephrolithiasis is attended with peculiar danger to life in cases of single kidney in which the stone occludes the ureter. Obviously, an effort should be made to remove promptly the calculus where single kidney is known to exist, after locating it by means of radiography. Indeed, the condition calls for unusual promptness if it is expected to save life. Obstruction of the ureter by a calculus has occurred after nephrectomy and has been relieved by timely nephrotomy. Complete occlusion of a single ureter tends to the development of uremia, ending in death. The operation should be done at the end of forty-eight hours if spontaneous relief is not afforded.

Says Ransohoff,[67] there are records of eleven operations of solitary kidney—four nephrotomies and seven nephrectomies. The nephrectomies were fatal in from one to eleven days. The case of Polk[68] lived eleven days. Traumatic rupture of a solitary organ caused death (as was to be expected) in a case reported by Taylor.[69] It is important to recollect that the ureteral orifice is generally absent on the side of the missing kidney. It follows that under these circumstances the condition under consideration is demonstrable by means of a cystoscopic examination; this should be, however, supplemented by catheterization of the ureters, in cases in which two ureteral orifices exist, since in a small percentage of the cases of congenital single kidney a rudimentary ureter is present, extending upward from the bladder for a variable distance. It is highly probable that in a certain proportion of the latter instances, at least, the catheter could be introduced into the ureter for a short distance, but obviously not any urine could be segregated.

The importance of single kidney from a surgical standpoint can scarcely be overemphasized. The subject is also of special interest to the pathologist and internist, as shown by the fact that the advanced lesions of chronic nephritis were found in 32 of the fatal cases, or 42.3 per cent. Finally, it cannot be doubted that the development of either acute or chronic nephritis in cases in which renal agenesis exists, gives a less hopeful outlook than when these arise under normal conditions, that is, bilaterally.

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DISCUSSION.

Dr. George Erety Shoemaker: The determination of this condition during life is a matter of very great importance to the surgeon. It happens to have been my duty to make this determination some three times in the last two months prior to nephrectomy for tumor, to nephrectomy for tuberculosis, and to operation without removal upon a large, painful dislocated kidney. The methods of determining whether the other kidney is present are four: First, to cut down upon it through the back of the abdomen. I believe this is the method which Kocher employs. The peritoneum is opened and the other kidney felt for. This is a certain method as to presence of the other organ, but does not prove its function, and it adds to the risk, as in many cases the kidney that is operated on is an infected one, and there is increased liability to infection of the peritoneum. If the kidney is cut down upon from the back and a horseshoe kidney is present, that fact may not be determined satisfactorily, because the exploration is not complete enough. A second method is catheterization of the ureters, referred to by Dr. Anders. This is not completely satisfactory because the introduction of a catheter into the ureter often inhibits partially the secretion of the corresponding kidney and causes error in diagnosis. Some urine escapes alongside the ureteral catheter at times, vitiating the determination of quantity.

A third method is that of so-called segregation, or forming two shallow urine pools in the bladder by an instrument which raises the bladder wall between the ureter openings. It is inexact when local changes make the tissues more rigid on one side than on the other and in no instance is it certain.

Another method, which is very practical and will nearly always succeed, is to inject into the muscular tissue of the buttocks a carmine solution, or give methylene blue by the mouth, and then watch with the cystoscope as blue jets of urine spurt through the different ureters. In cases in which this has been done, within seven to eighteen minutes there was a very definite spurting of the blue urine into the clear water previously placed in the bladder. It makes a perfect demonstration of the presence of a kidney on that side, and it would require the ureter to cross the spine to become fallacious. In another patient there was a very slow expulsive action on one side and a rapid succession of spurts on the other. That would differentiate the two kidneys, as to relative activity, as the procedure exercises no inhibition on either side.

Dr. Alfred Stengel: I should like to ask Dr. Anders what the figures are of the frequency of two ureters coming from a single kidney. I have once seen at autopsy a single kidney with two ureters, and I can readily see how a surgeon using a catheter might be deceived in thinking there were two kidneys, and might undertake operation. It might be of interest to know how frequently this anatomical condition has occurred in the very elaborate statistics

which Dr. Anders has collected. It might be possible in unilateral kidney that one ureter might cross and open on the side of the bladder opposite the single kidney. In such a case the only kidney might be removed.

DR. ANDERS, closing: In answer to Dr. Stengel's query, I can only say that in cases of horseshoe kidney two ureters are commonly present, and also duplication of the pelvis of the kidney is often observed. On the other hand, in a true, congenital single kidney one ureter was the rule, and I do not recall a single instance in which two ureters beginning in the bladder and extending up to the kidney occurred under these circumstances. As I said, in a small percentage of the cases there are two ureters. The one on the side of the missing kidney extends upward for a short distance only, and it is not connected with any renal tissue above.

It is a significant fact that one person in every 1817 should be subject to congenital single kidney. If we add rudimentary kidneys, and kidneys atrophied as the result of disease, the ratio would at once rise very much higher. Under these circumstances the importance of knowing the presence or absence of "single kidney" in every individual must be apparent. This can be done in the vast majority of cases as the result of simple cystoscopic examination. However, where two ureters exist, the investigation should not stop there. One of the different methods—either catheterization, or, if not satisfactory in its results, other methods, including those mentioned by Dr. Shoemaker—should be employed. A considerable number of the cases to be found in my tabulated lists died of ureteral calculus, and many of these would have been saved had the existence of a single kidney been known beforehand.

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EXTRASYSTOLIC ARRHYTHMIA SIMULATING HEART BLOCK.[1]

A REPORT OF SOME CASES, ONE OF WHICH WAS OF UNUSUAL INTEREST.

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This article has been prepared for two reasons: (1) Because of the interesting and unusual character of the sphygmograms from Case I, and (2) to call attention to the similarity, and to point out the differences, between the above-named two conditions. A proper differentiation is not merely of academic interest, but of extreme practical importance, since both prognosis and treatment differ radically, according to which of the two forms of cardiac irregularity we are dealing with.

An extrasystole has been defined by Mackenzie as "a premature contraction of the auricle or ventricle in response to a stimulus from some abnormal point of the heart but where otherwise the fundamental or sinus rhythm of the heart is maintained."

The modern conception of cardiac physiology regards the rhythmic contraction of the heart as autogenetic. That is, although it is influenced and modified by nervous impulses, it is primarily independent of these factors. Under normal circumstances the stimulus to contraction arises at the mouth of the large veins near the point of their union with the right auricle, apparently in a small remnant of embryonal tissue—the remains of the venous sinus of the primitive cardiac tube.

[1] Read October 6, 1909.

From this point the stimulus passes by direct muscular continuity from cell to cell along the auricular walls to the auriculoventricular bundle (His' bundle, Gaskell's fibers) and then to the ventricles. In its passage from the right to the left heart the stimulus evokes a contraction of the chambers through which it passes. According to Engelmann the contraction passes through different parts of the heart at a varying rate, a condition which favors more complete emptying of the chambers.

Immediately after the systole, the heart muscle is in what is termed the refractory phase. That is, it will for the time being respond to no further stimulus; but during diastole the refractory condition gradually passes off, and if a second stimulus now arises before the next normal stimulus is due, a premature contraction—extrasystole—occurs. This extrasystole is also followed by a refractory period, and so it often happens that the next normal contraction stimulus produces no contraction. Thus, a "beat is missed" and a pause ensues which lasts until the third normal stimulus occurs, unless the rhythm is again disturbed by the occurrence of a second extrasystole. In the former event we get a typical pulsus bigeminus, two close-coupled contractions followed by a long pause. The later the extrasystole occurs after the regular contraction the longer will be the pause which follows it. By virtue of these long—compensatory—pauses the cardiac rate per minute may remain unchanged, despite the regular occurrence of extrasystoles. Thus, the interval of time occupied by the normal contraction and the extrasystole plus their respective pauses will be the same as would that of two normal cardiac cycles. This state of affairs occurs characteristically in cases in which the extrasystole has its origin in the ventricle; it may also occur when the extrasystole arises in the auriculoventricular node or bundle; it does not occur when the point of origin is at the sinus.

Now, an extra stimulus may arise at the sinus, in the auricular walls, in the ventricular walls, in the auriculoventricular node or bundle, and may produce a premature contraction of one or more chambers of the heart. Such a condition is naturally apt

to interfere with the next normal stimulus as it comes down from the sinus.

Sometimes, however, when the cardiac rhythm is slow, an extrasystole may occur which has no compensatory pause, and does not interfere with the next regular beat. This is then termed an interpolated extrasystole. The rarer form of paroxysmal tachycardia may be produced in this way.

When the extrasystole produces a small peripheral wave, we get a pulse irregular both as to time and volume. If it occurs early and entirely fails to produce a peripheral wave, we get an intermittent pulse. Quite often the two conditions are blended, so that while feeling the radial pulse we note, now a very small feeble wave, now a complete intermission. Very frequently, too, when the finger notes only an intermission, a sphygmographic tracing will show a faint arterial elevation. Although the radial and even brachial tracing may thus show no pulse as the result of an extrasystole, the cardiogram, of course, will do so. In the jugular tracing, too, we are apt to have a well-marked wave. The right heart is still engorged with blood, but little if any more can be taken in from the cavæ, so when the right auricle and ventricle contract as the result of the extrasystole, they will produce a large presystolic and systolic venous wave, owing to the blood which has accumulated during the last auricular systole, which has been steadily flowing toward the heart and now finds no avenue of inflow. The fallaciousness, therefore, of merely palpating the radial artery in cases of arrhythmia is plainly evident. One should always ascertain whether the radial pulses correspond in point of frequency and force to the impulse of the cardiac apex and to the heart sounds.

Knoll was able to produce extrasystoles in the dog's heart by constricting the aorta. It seemed, therefore, that a disproportion between the work to be done by the heart and the functional capacity of the same had induced the condition. This was further corroborated by the fact that extrasystoles occur in man under conditions of high arterial tension when the heart is beginning to show signs of being no longer able to cope with the abnormally

high blood pressure. There must, however, be some other factor concerned in the production of the condition, otherwise we should see extrasystoles in all cases of failing compensation in heart disease, which is, of course, not the case. If an extrasystole follows a normal contraction, it is often followed by a compensatory pause, due to the fact that when the second regular stimulus comes along, the heart is still in the refractory phase produced by the extrasystole. In this manner the second regular systole is dropped, and not until the third is due do we have another contraction. Now why do we not have a second extrasystole following the first, during the long pause which followed it. If the abnormal stimulus is constantly present, as Mackenzie believes, we should expect a second extrasystole during the compensatory pause. If, on the other hand, it is a temporary condition, as Lommel holds, why do they recur so soon and so regularly, as is often the case? Korányi suggests that the abnormal stimulus is constantly present, but in varying degree; and since the extrasystole is generally followed by a long pause, it seems likely that extrasystole itself temporarily supresses the underlying tendency which produced it. The later the extrasystole appears, the longer the time it occupies, and the longer the postextrasystolic pause. Therefore, the stronger the extrasystole, the longer will the stimulus which provoked it be abated. Inasmuch as this relation is apparently based on the strength of the systole, Korányi argues that the origin of the extrasystole is probably of a mechanical nature. Long pauses, then, are apt to follow late extrasystoles. If the former last until the next normal stimulus arrives, they are naturally followed by a regular contraction, and therefore all but very early extrasystoles must sooner or later be followed by normal systoles.

A gradually increasing aortic pressure first calls forth the normal reserve capacity of the heart. When this is overequalized by the work to be accomplished, the systolic output falls, and the ventricle is incompletely emptied. Finally, when intraventricular pressure remains high enough during diastole it may act as an extra stimulus. It has been repeatedly and satisfactorily

demonstrated that such intracardiac pressure may produce this result. A compensatory pause (long diastole) allows the other heart chambers to empty their contents so that the circulation can be carried on. This manifestly is only possible if the different chambers are each handling the same amount of blood. Furthermore, the long pause giving the ventricle a better rest is followed by an increase in contractility and hence a better systolic output. Thus it may happen that the occurrence of extrasystole has actually a conservative and beneficial effect upon the circulation, by adjusting the relationship between the strength of the ventricle and the arterial pressure to be overcome. Korányi maintains that extrasystoles only occur when different heart chambers are variously affected in the extent of their incapacity. If all of the chambers are equally involved, no one of them can cause a hyperdistention of any of the others, and therefore, no extrasystoles can occur. This is further corroborated by the fact that the occurrence of extrasystoles bears no constant or definite relation to the extent of the dilatation; and by the fact that extrasystolic arrhythmia often disappears in the preagonal stages of broken compensation; whereas irregularity often returns hand in hand with improvement of the patient. This explanation is, of course, not applicable to all varieties of extrasystolic arrhythmia, but only to those in which the tracings show that the postextrasystolic pauses increase hand in hand with the force. In these cases we are dealing either with the mechanical effects of valvular disease or with a pathologically altered state of a certain one of the cardiac cavities. From a clinical standpoint there is every reason to believe that extrasystoles may also be produced through nervous influences, although this statement is not accepted by some physiologists because extrasystoles cannot be brought about experimentally through nerve stimulation.

If the extrasystole occurs very soon after the normal cardiac contraction the ventricle will be insufficiently rested; will contain little blood (except in cases in which the extrasystole results from overdistention); whereas the aortic pressure will still be high. As a result, it may be that, although the ventricle contracts,

it barely, if at all, opens the aortic valves; and hence a pulse wave will not be transmitted to the periphery, and perhaps not even to the larger vessels. This is commonly spoken of as an intermittent pulse. Now, the ventricle when it does contract under these conditions may or may not give forth an audible sound. Generally it does so, and the sound thus produced has been described by the Germans as the "paukende ton" (kettle-drum tone) of the extrasystole. The later the extrasystole occurs in the diastolic period the louder will be the sound it produces, and the more likely will this sound be followed by valvular sound (produced by the sudden tension of the aortic and pulmonary valves). The sound of an extrasystole is generally muffled, low pitched, and indistinct. As a rule, it follows closely upon the normal second sound of the heart; when, however, it occurs later in diastole it may be mistaken for the auricular contraction, such as occurs in cases of heart block. In such a case, however, it would not be accompanied by an impulse of the ventricle on the chest wall. It has been shown by Hochhaus and Quincke that the extrasystolic sound may be heard either over the whole heart or only localized to some part of it. Korányi[1] has called attention to the fact that it is best heard over whichever one of the cardiac chambers are most concerned in maintaining compensation. Thus, in arteriosclerosis, interstitial nephritis, plumbism, aortic lesions, etc., is it loudest over the left ventricle, and from thence outward toward the axilla; whereas the extrasystolic tone of the right ventricle is much weaker. On the other hand, in mitral disease, emphysema, etc., when the right ventricle is greatly dilated the extrasystolic sound is best heard clearly over the whole precordium (the space occupied by the right ventricle) except at the very apex and to the left of it. Occasionally, however, it is heard clearly at the apex in mitral disease in those cases in which the hypertrophied and dilated right ventricle occupies the whole anterior aspect of the heart.

Extrasystoles are generally classified according to the location

[1] Med. Klinik, September 13, 1908, p. 1403.

at which they originate, as (1) auricular; (2) auriculoventricular; (3) ventricular. As a general rule, we can definitely determine which of the three varieties we are dealing with by certain characteristics of the pulse tracings. Thus, in the first variety the extrasystole is preceeded by an "a" wave in the jugular pulse and is not followed by a compensatory pause. In the second variety the auricle and ventricle contract at or nearly the same time, hence a very large "a" (a-v) wave is produced. The compensatory pause may, or may not, occur. In the third variety the extrasystole is not preceeded by an "a" wave, and the compensatory pause is not only present, but frequently prolonged.

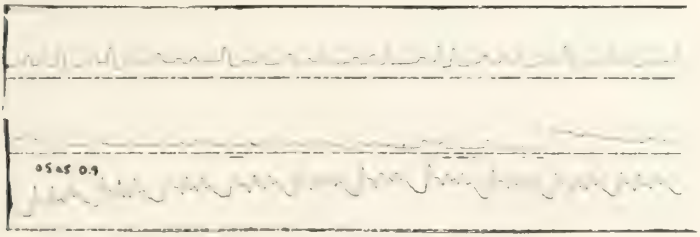
Mackenzie[1] has lately promulgated the hypothesis that the stimulus for contraction may arise in the remains of the embryonic primitive cardiac tube, assuming that this tissue might preserve the functional peculiarities of the original tube. Such tissue is to be found at the mouths of the large veins in the right auricle, in the auricle, in the A-V node and in the A-V bundle after it leaves the node. He makes a sharp distinction, however, between extrasystoles arising in the A-V node occasionally, and what he has described as "nodal rhythm," in which all the contractions start at this point, and in which, therefore, there is no fundamental sinus rhythm whatever. Not rarely, it happens, that a number of extrasystoles follow one another, and thus we get what has clinically long been recognized as pulsus bigeminus, trigeminus, quadrigeminus, etc., according to the number of extrasystolic beats which are felt or heard before the long pause.

Tracing A illustrates a *pulsus trigeminus*, and was taken from a case of aortic insufficiency a few days before death. Here we see a normal contraction followed by two extrasystoles, the second one of which shows a compensatory pause.

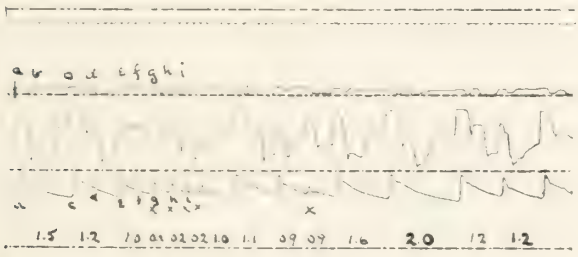
Tracing B shows four extrasystoles occurring in rapid succession. It was taken from a patient suffering from mitral and tricuspid insufficiency, who died quite rapidly three days later from œdema and congestion of the lungs. The jugular tracings show the large systolic wave of tricuspid insufficiency.

[1] Diseases of the Heart, 1908, p. 145.

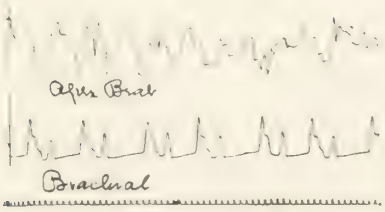
Tracing C shows a typical *pulsus bigeminus*. It was taken from a middle-aged woman who had long suffered from mitral and tricuspid valvular disease, the result of an antecedent rheumatic polyarthritis. At the time this sphygmogram was made compensation was very bad indeed. The apex beat shows the systolic retraction characteristic of an hypertrophied and dilated right ventricle.



Tracing A



Tracing B



Tracing C

Case I.—J. St. (Philadelphia Hospital, patient of Dr. A. A. Eshner), white, male, single, pedler, aged fifty-eight years.

Chief Complaint. Dyspnea, palpitation.

Personal History. Variola in infancy, complicated by an inflammation of the right eye. Enteritis at eighteen years. Has been much exposed to the weather, and carried heavy packs. Has never used tobacco; and has used no alcohol since the age of twenty-one years. Denies venereal infection, but has evidences of an old keratitis in his left eye. His health has always been excellent.

Present Illness. On the evening of March 11, 1909, after walking perhaps thirty feet, he was suddenly forced to sit down on account of weakness, dyspnea, "nervousness," and cardiac palpitation. He had never had such an attack before. This condition persisted until he was admitted to the hospital the next day.

Physical Examination. A well-built and fairly nourished man. Pallor marked. Pulse, 120; temperature, 100°; respirations, 35. Very marked arcus senilis, also thickening of all the peripheral arteries.

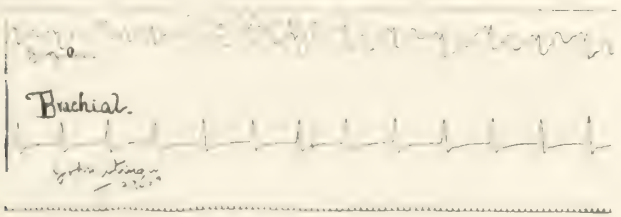
Lungs. Over an area about the size of an orange, near the left nipple, there is a peculiar harsh jerky inspiration. Otherwise negative findings.

Heart. Apex beat neither palpable nor visible. A diffuse undulating epigastric impulse is noted. Heart dulness seems about normal. The sounds are weak and distant, and the action very irregular. Variable and inconstant aortic and mitral murmurs are heard. "Arrhythmia is the predominating feature."

Urine. Chemically and microscopically shows nothing important.

Blood. Hemoglobin, 70 per cent.; erythrocytes, 5,120,000; leukocytes, 9200. The patient was given 10 minims of the tincture of digitalis four times daily. About one week later it was noticed that the patient's pulse had dropped suddenly from about 80 to 40 beats per minute. Furthermore, neither rate remained constant for any great length of time, but when the rate did vary it always did so by doubling or halving, at least approximately. On auscultation of the heart during the higher rate nothing abnormal was heard except what has already been described. During

the slow rate, however, a distinct, distant, muffled third sound was heard, occurring so late after the normal second sound that there could be no question of a mere reduplication of the latter. In character this abnormal third sound was apparently of muscular origin, but it was not followed by a valvular sound. Synchronous with the third sound there was a well-marked pulsation in the somewhat prominent jugular veins. About this time I first had an opportunity of studying the case through the courtesy of Dr. Eshner. A pulse tracing was taken which is here reproduced. The apex beat appearing very feebly upon the chest wall, only the jugular and brachial tracing was recorded.

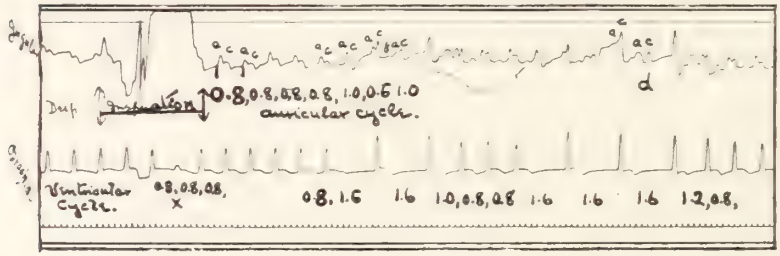


TRACING I

The brachial rhythm is regular. The jugular shows the three normal waves (A-C-F) occurring in normal relations with the arterial pulse in the brachial; but in addition to these waves there is interpolated, between every two brachial pulses, a third wave in the jugular which does not correspond to any arterial wave, and which appears with great regularity every seven-tenths of a second, or just twice as often as the brachial pulse. The tracing therefore, upon cursory inspection appeared to corroborate the clinical diagnosis of heart block. It may be stated that the patient suffered no discomfort, and did not even seem conscious of the change of the heart rhythm. While in the hospital he had no vertigo or syncopal attacks, and was only conscious of occasional palpitation.

During the course of the next week I made a number of tracings, being much interested in the frequent and sudden change in the rate of the pulse. I believed at the time that we were dealing

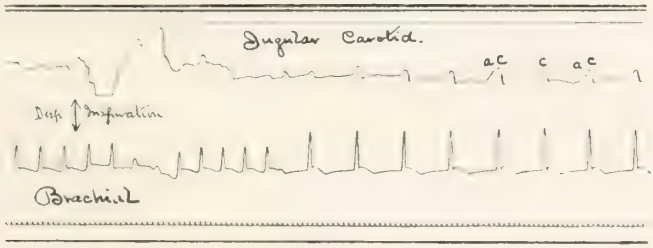
with a case of heart block, probably due to sclerosis of the auriculo-ventricular bundle, and possibly precipitated by the action of digitalis. Complete withdrawal of the drug for three days, however, had no effect on the condition. When the patient was up and about the ward his pulse was more frequently in the eighties and when recumbent in the forties. He said that he felt well, and was anxious to be out of bed as much as possible. For purposes of more careful study, however, he was put back to bed and kept there continuously for a couple of weeks. During this time it was found that *the pulse rate could be made to vary almost at will* by a few simple procedures. Thus, for instance, sitting up in bed and then lying down again would reduce the rate from 80 to 40. The taking of from one to three forcible inspirations and expirations invariably had the same effect. Sometimes the rate would remain low for several minutes, at others the low rate would only continue for a certain number of beats. As time went on there was less and less tendency for the low rate to remain for a long time. The blood pressure varied but was generally about 138 mm. Hg. systolic, and 100 mm. diastolic.



Tracing II

Tracing II, taken at a later date than Tracing I, clears up the question. Here will be seen the effect of a deep inspiration upon the brachial pulse. First a very small systole occurring at the normal time and then after six regular systoles an occasional dropping out of every other beat in the brachial. This tracing was taken during the latter part of our study, and shows the

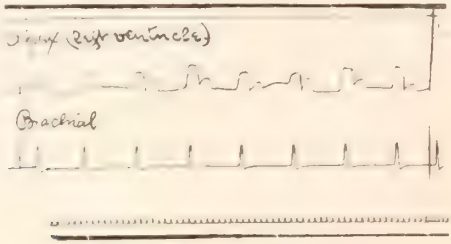
tendency already mentioned for the slow rhythm to be very transient. In the early tracings an inspiration of this kind would produce a continuous slow rate, such as is shown in the last half of Tracing III. It was a curious fact, which was almost invariably noted, that the deep inspiration was not immediately followed by a change of rate, but that this occurred only after from three to six beats. The small brachial wave immediately following inspiration in Tracing II (*X*) might be accounted for mechanically by the suction action of the lungs, which would cause more blood to be temporarily retained in the pulmonary vessels, and consequently less to reach the left ventricle. The jugular tracing of No. III, is unsatisfactory, and only occasionally shows both the "A" and the "C" waves.



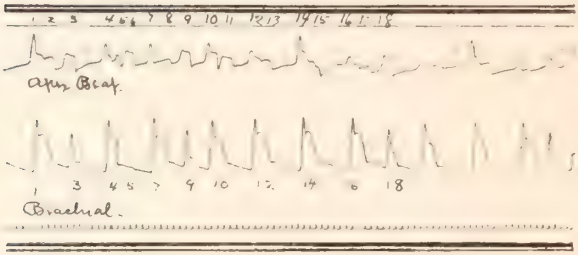
TRACING III

A further study of the jugular pulse in Tracing II also clearly demonstrates the fact that the supernumerary "A" wave noted in the first tracing is really composed of two waves –"A" and "C"—in other words, simply a repetition of what occurs normally a contraction of the right auricle and right ventricle. Now, the question arose were we dealing with a case of hemisystole, in which the ventricles did not contract simultaneously, and in which perhaps the left ventricle did not contract at all? There is still much doubt as to whether hemisystole occurs in man, although some good authorities consider that its occurrence has been demonstrated. (The majority, however, if not all of the reported cases, can be explained in another way.) A tracing was therefore taken from the apex beat to show that the left

ventricle did contract regularly after the auricle. Tracing IV shows very distinctly the double, close coupled contraction of the left ventricle (it was taken at the outermost part of the apex impulse), only the first one of which is followed by an arterial (brachial) pulse. This type of cardiogram is typical of extrasystolic arrhythmia.



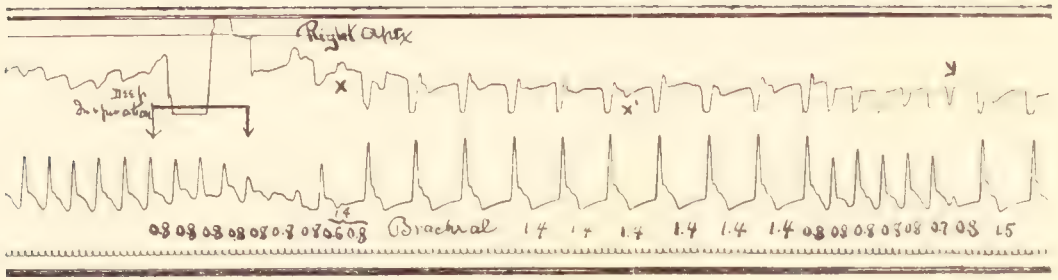
TRACING IV



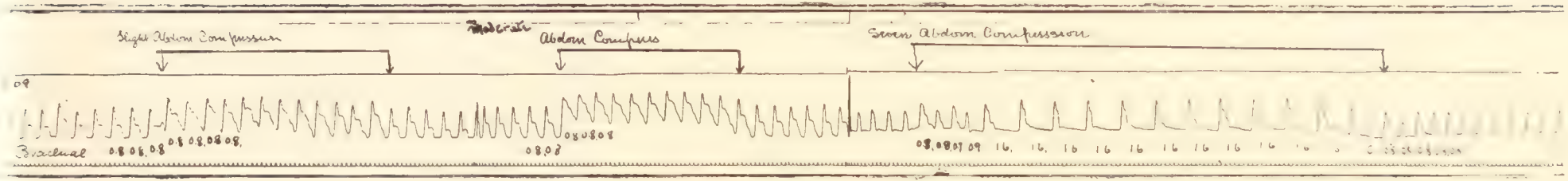
TRACING V

Tracing V taken at a still later date is a quite typical example of extrasystolic arrhythmia. Here the apical systoles Nos. 2, 5, 11, 13, 15, and 17 are not followed by brachial pulses; while systole No. 6 produces such a small wave that it probably would not have been perceptible to the finger, and certainly would not have been so in the radial artery.

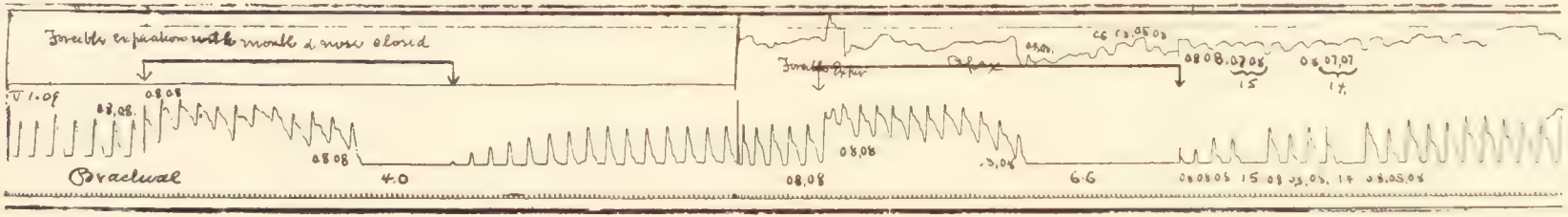
Tracing VI was made from the brachial artery and the innermost part of the apex impulse. It shows very distinctly the systolic retraction of the right ventricle, as well as depicting the appearance of extrasystolic pseudobradycardia for eleven successive beats shortly after a deep inspiration followed by a forcible



TRACING VI



TRACING VII



TRACING VIII

expiration, and then for a period of six beats the regular rhythm, which again lapses in the condition of pulse intermission.

It was generally very difficult in this patient to get a satisfactory cardiogram. Hence it is that the extrasystoles occurring between the brachial pulsations do not appear except at the points marked *X*. In view of the fact, however, that this was the only form of arrhythmia noted at this time among nearly one hundred tracings which were made, it seems reasonable to ascribe the brachial intermissions to this cause.

Tracing VII was made at the suggestion of Dr. Lodholtz, of the Physiological Department of the University of Pennsylvania, to determine, if possible, to what extent the sudden change of rhythm was the result of increased blood pressure, *i. e.*, work thrown upon the heart. The first part of the tracing was taken from the brachial artery while the patient was resting quietly in bed. At the point marked by the arrows sudden pressure was made upon the patient's abdomen with both palms by my assistant,[1] with results which are graphically demonstrated in the sphygmogram. Slight pressure simply elevated the height of the tracing. Moderate pressure produced still more elevation; but severe pressure completely changed the rhythm of the arterial tracings to one-half their previous frequency, a condition which persisted until the abdominal compression was stopped, when a regular though somewhat more rapid rate (than before the experiment) was established.

Tracing VIII shows the effect of Valsalva's experiment (forcible expiration with the mouth and nostrils closed). Here it will be noted that in both the trials after a primary and marked elevation of the blood pressure there occurred, after eleven and twelve cardiac contractions respectively, a complete disappearance of the brachial pulse, which lasted as long as the breath was held. Following the second trial there is in some places a complete dropping out of brachial pulses. Both of these trials exemplify a marked exaggeration of what occurs with normal individuals during

[1] Dr. Keilty, to whom I am indebted for aid in making these sphygmograms.

Valsalva's experiment. In healthy individuals the pulse does not disappear so soon nor so completely. It occurred to me after making these tests that perhaps *this method might be used to determine the functional capacity of the heart*, by having the person who was being tested hold the breath for a given time, and comparing the tracings thus obtained with an average normal standard. The trouble would, however, lie in having the same amount of compression exercised upon the splanchnic vessels by the abdominal muscles. I hope, however, to make some further observations and to report upon this question in the future.

As to the exact effect of the Valsalva experiment upon blood pressure in human beings, Bruck[1] has shown that there occurs an immediate rise averaging from 30 to 40 mm. Hg., followed by a fall of pressure to or below the normal, and this in turn is succeeded by a secondary rise to a point above the normal, but not as high as the primary rise. Both the last-named author and Schlippe[2] demonstrated by means of an œsphageal tube a positive intrathoracic pressure ranging between 50 and 120 mm. Hg. during similar experiments. Their results can, in a measure, be corroborated by inspection of the rise and fall of the base line of Tracing VIII, in which the primary and secondary rise of pressure and the intermediate fall during the Valsalva experiment are clearly shown. The complete disappearance of the brachial pulse during the latter part of the experiment is in part, at least, due to the fact that while forcible compression of the intrathoracic space is maintained, the venous blood flow from above the clavicles and from below the diaphragm into the cavæ is prevented, and hence the heart chambers and the lungs being once emptied there is no more available blood for the heart to pump to the periphery.

A further attempt was made to have the patient reverse the process, attempting to inspire with the mouth and nostrils closed, and thus diminish intrathoracic pressure, but the results were the

[1] Ueber den Blutdruck bei ploetzlichen starken Anstrengungen und beim Valsalva'schen Versuch., etc. Deut. Arch. f. klin. Med., August 6, 1907, vol. xci.

[2] Ibid., vol. lxxvi.

same as with forcible expiration, and inasmuch as with normal individuals the results are quite different, we assumed that the difficulty lay in the fact that the patient compressed his abdominal muscles instead of merely drawing down his diaphragm.

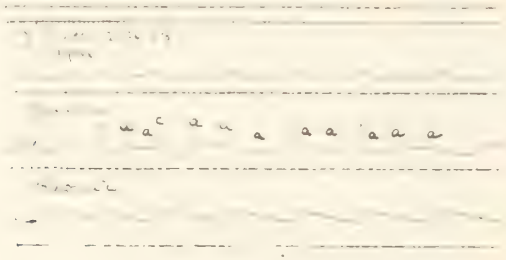
Our patient belongs to that class of cases to which Wenkebach[1] has called particular attention, and regarding which he questions whether we are dealing with extrasystole at all. Extrasystoles, he points out, do not, as a rule, occur regularly, but are apt to appear at irregular intervals. In Case I we find during the brachial intermission an extrasystole which appears regularly after each normal contraction. Furthermore, once the extrasystoles cease, they cease suddenly and entirely. He suggests that, inasmuch as there are no compensatory pauses, the extrastimulus must arise at the venous ostia "a conclusion which at once makes it doubtful if they are in the nature of extrasystoles." Wenkebach may, however, by this time have changed his views, his work having been published in 1904. Unfortunately, however, he gives no venous tracings, so that instead of definitely knowing the site of origin, this point can only be surmised. In our case, however, it is clearly shown that in Tracing V the extra stimulus arose in the auriculoventricular bundle or node; whereas in Tracing II both the auricle and the ventricle contract in normal time relationship, except at "d" where there is a delay of conductivity, the A-C interval measuring four-tenths of a second. In Tracing V the extra stimulus must have arisen in the auriculoventricular bundle or node, inasmuch as compensatory pause is lacking (the extrasystoles appear midway between the regular contractions), and the jugular pulse at this time shows a large, single summation wave, which results from the simultaneous contraction of the right auricle and ventricle.

A further reason for believing that the peripheral pulse intermissions in our case were extrasystolic in origin lies in the fact that extrasystoles *did* appear irregularly in some of the tracings, a fact which Wenkebach states is very unusual in those cases which he differentiates as being a "true bigeminy." The case

[1] Arrhythmia of the Heart, London, 1904, p. 45.

is clearly not one of auriculoventricular heart block, as was first supposed, because the jugular pulse at the time of the extrasystole shows a "c" wave as well as an "a" wave, and, furthermore, because the tracings from the apex beat show that both the right and the left ventricle contract regularly with every extrasystole.

For purposes of comparison a tracing from a case of true heart block is herewith reproduced, which shows single auricular waves occurring at fairly regular intervals and bearing no definite time relationship to either the apex beat or the radial pulse. The case being one of complete block, there is no "A-C" interval by which to measure the conductivity time, because the auricles and ventricles are beating independently and incoördinately (Tracing IX).

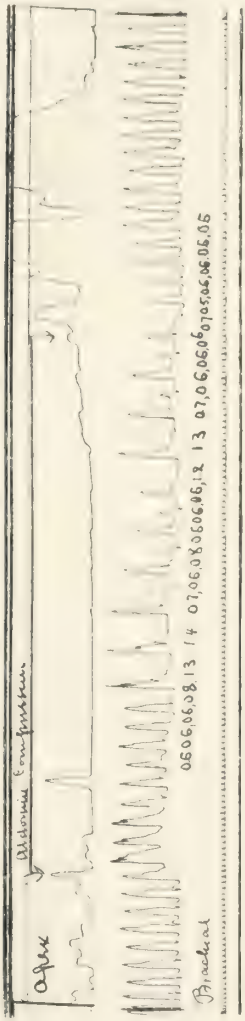


Tracing IX

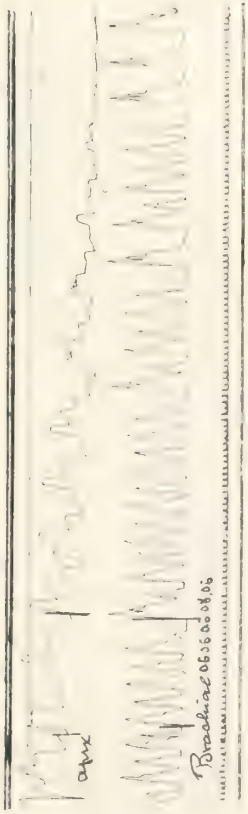
Three weeks after the patient had left the hospital I was again able to make some tracings. During this time he had had no medication whatever. He was up and about, doing some light work. He had constantly more or less dyspnea and was unable to stand prolonged exertion of any kind. Pulse rate, 100; systolic pressure, 140 mm.; diastolic, 90 mm. Tracing X was made at this time. Forcible inspiration and expiration no longer produced any extrasystoles, although severe pressure upon the abdomen was followed by a few, most of which, however, were followed by small brachial pulses. The compression experiment was made a number of times, but after the first attempt failed to bring on any pulse intermissions.

The patient was again ordered to take 5 minims of tincture of digitalis thrice daily. One week later Tracing XI was made.

At this time he was frequently having extrasystoles, both in the erect and in the recumbent postures. His blood pressure was



TRACING X

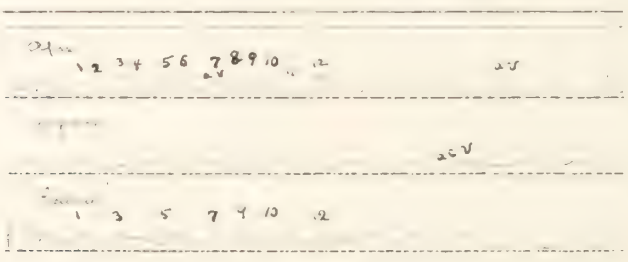


TRACING XI

considerably higher (systolic, 170 mm.; diastolic, 100 mm. erect; systolic, 145; diastolic, 90 mm. recumbent). Pulse, 90 per minute.

Tracing XII was made one week later, the patient having

meantime been taking 5 minims of tincture of belladonna four times daily instead of digitalis. He had had no more attacks of palpitation. His blood pressure, while erect, was 110 mm.; diastolic, 90 mm. Recumbent, 120 mm.; diastolic, 90 mm.; distinctly lower, therefore, than at the previous examination. The brachial Tracings, XI and XII, show a very distinct alternating action on the part of the left ventricle—a large and then a small beat, of nearly equal duration regularly following each other. From time to time an intermission occurred in the brachial pulse, as at (X), which was in turn followed by a large powerful systole.

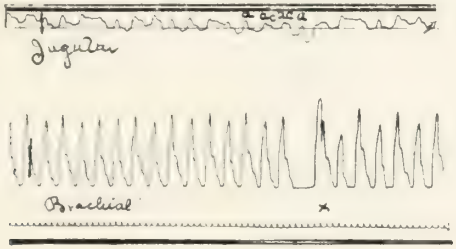


Tracing XII

At this time neither deep breathing nor abdominal pressure, nor the Valsalva experiment produced any arrhythmia. The pulsus alternans, which is also plainly evident in Tracings X, XI, and XII, is evidently the expression of myocardial weakness, resulting from myocarditis, a part of this patient's advanced general arteriosclerosis.

Tracing XIII was made one week later, the patient having taken the tincture of belladonna as last mentioned. He had done some physical labor the same morning. When seen in the afternoon dyspnea and pallor were extreme. Pulse, 90; respiration, about 40. Facial expression showed marked anxiety, and he complained of severe precordial pain. Shortly after the tracing was completed, the patient's condition having gone from bad to worse despite the administration of strychnine and ammonia, he was hurried to the Pennsylvania Hospital apparently in a moribund state, since he was rapidly developing very marked

edema of the lungs and was suffering severe anginal pain. His life was apparently saved, however, by free hypodermic administration of atropine, strychnine, and morphine, and when seen in the ward one week later his condition seemed no worse than it had been two weeks before. He was able to walk a little, although dyspneic, and his pulse tracings showed a typical regular pulsus alternans, without extrasystoles very similar to that seen in Tracing XIII.



TRACING XIII

The cause of the pulse intermissions in this case was apparently an increase of arterial pressure; at least this factor was constantly present in every instance in which they were either artificial or naturally induced. There can be little doubt, however, that the administration of digitalis played an important role in their production, since they disappeared after the prolonged withdrawal of the drug and reappeared promptly after its resumption. Thus, for instance, when the abdomen is forcible compressed there results an immediate and marked rise of arterial tension. Again during the performance of the Valsalva experiment we have a similar rise of arterial pressure resulting from contraction of the abdominal muscles, and a further strain put upon the heart by the fact that the right heart has much greater difficulty in forcing the blood into the contracted and compressed lungs. As to the occurrence of pulse intermissions when the patient lay down, and their disappearance when he stood or sat up, here again we have to deal with a higher arterial pressure in recumbency. An additional reason doubtless lies in the fact that when standing

or walking the normal sinus rhythm is more rapid, and hence there is less likelihood that an abnormal stimulus will be generated in the pulse intervals, for it is a well-known fact that extrasystoles are much more apt to occur when the rate of the heart is slow.

Digitalis may induce the occurrence of extrasystoles in two ways: (1) By increasing arterial tension, which it seemed to do to an unusual extent in this case; and (2) by slowing the sinus rate of the heart and thus indirectly favoring extrasystoles by prolongation of the diastolic interval. This explanation is in a measure satisfactory, but, on the other hand, we are confronted by the apparently paradoxical fact that one of the most important effects of digitalis on the heart is an increase in tone; and it has been shown that when tone is increased, contractility, conductivity, and probably excitability are diminished.[1] Now, if digitalis decreases excitability, it ought to decrease the tendency which causes the extrasystoles, instead of which it had a diametrically opposite effect. This is perhaps due to the fact that in the case in question the effect of the drug upon the arterial tension was so marked that this factor more than counterbalanced the depression of excitability. Furthermore, we must bear in mind that most of the experimental work on digitalis has been done on the hearts of healthy animals, whereas the effect of this drug upon a diseased human heart is in all probability more or less different.[2] For instance: "Mackenzie has shown that a normal heart, or a diseased heart which is not at the same time dilated, is practically unaffected by such doses of digitalis as can be given to men by mouth. This is perhaps only what should be expected, since it is probable that a smaller dose would be required to increase the tone of a dilated heart (*i. e.*, where tone is much diminished) than to add to the tone of heart where it is already at the normal standard. The excitability of tone varies with different circumstances in animals, and no doubt has the same variability in human beings. It is in cases of recent dilatation, or recent increase

[1] Gossage, Proc. Royal Soc. of Med., July, 1908.

[2] Cushny states that digitalis increases the irritability (Heart, 1909, i, 21), but we must bear in mind that in the human being the effects of this drug on the heart muscle are to a large extent masked by its effect on the pneumogastric nerve.

of dilatation, where the muscle is healthy, that the tone of the human heart seems especially susceptible to the influence of digitalis" (Gossage). It seems likely also that the vagus nerve played an important role in the production of the extrasystoles in our case. The arrhythmia was apparently closely connected with, and certainly was very much increased by the use of digitalis, which drug, as is well known, stimulates the pneumogastric nerve. Atropine, on the other hand, acts as a vagus depressant, and its administration almost caused a disappearance of the extrasystoles, even under conditions in which the blood pressure was markedly increased.

As a summary of what has been learned from the foregoing lengthy and detailed study of this very unusual and, in some respects, paradoxical case, I would submit the following:

We have been dealing with a case of myocarditis. This is evidenced by the physical examination, by a marked limitation in the field of cardiac response, and by the pulse tracings, which showed at times a marked delay of conductivity and also a typical pulsus alternans, both of which conditions are of bad prognostic import. The patient was suffering from a very atypical form of arrhythmia, which was clinically manifested by a disappearance of every other arterial pulse wave, thus suddenly and often, for a considerable interval of time halving the pulse rate. This arrhythmia could, for a period of about three weeks, be brought on at will by deep breathing and other simple procedures, and was apparently always associated with, and at least, in part, the result of, increased blood pressure. We are positively not dealing with a case of auriculoventricular heart block. The administration of digitalis invariably made the condition worse, and sometimes seemed to be the direct cause of it. The effect of belladonna, on the other hand, seemed to be beneficial, and considering the diametrically opposite effect of these two drugs on the vagus, suggests that this nerve may have played an important part in the production of the arrhythmia. Certain reasons may be advanced for believing that we were not dealing with extrasystolic arrhythmia properly understood at all, but with the condition which has been designated as "true bigem-

inus;" the close-coupled contraction of left ventricle in Tracing IV, as well as the auscultatory examination of the heart, would, however, seem to contradict this belief. We personally believe that the form of the arrhythmia varied at different times, and that sometimes we were dealing with "true bigeminus," at others with undoubted extrasystoles. One other explanation, however, seems possible, i. e., the peripheral pulse intermissions simply resulted from an extreme degree of myocardial weakness, which caused the small waves of a pulsus alternans to drop out entirely. We have never seen such a case described, but can see no reason why such a state of affairs should not be perfectly possible.

Case II.—Mrs. McG., white, aged thirty-one years, married, housework.

Diagnosis. Mitral obstruction and insufficiency; tricuspid insufficiency; hypertrophy and dilatation of the heart.

Chief Complaint. Edema of the extremities, cough, and dyspnea.

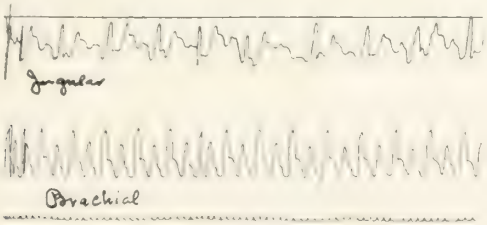
Personal History. Severe attack of rheumatic fever at age of twelve, ill for six months. Has had attacks off and on ever since. Typhoid fever at seventeen. Malaria at eighteen. When nineteen years of age she was told she had a "bad heart," but had no subjective symptoms, and regarded herself as well until the birth of the last child, two years ago. During pregnancy compensation had been well maintained, but immediately after delivery, dyspnea, edema, cough, pallor, and weakness had set in.

Physical Examination. Marked emaciation, orthopnea, cyanosis, edema of the extremities. A slight tuberculous involvement of the right lung, apical, with tubercle bacilli in the sputum.

Heart. Dulness much increased to both right and left. Apex beat displaced outward and downward. A presystolic thrill within the apex impulse, which is forcible and rather diffuse. There is marked pulsation of the distended jugular veins. A loud harsh systolic murmur almost entirely displaces the first sound at the apex, and is transmitted to the axilla. A faint presystolic murmur is also heard. The striking feature of the case is the coupled rhythm of the heart. Two systoles occur in rapid

succession, followed by a prolonged pause. The second systole is occasionally followed by a second (valvular) sound, but by no means always. The first systole produces a well-marked radial pulse, the second does not.

The liver is not demonstrably enlarged. The urine contains considerable albumin, and microscopically shows granular and hyaline casts.



TRACING XIV

The pulse Tracing XIV shows a typical bigeminal action on the part of the left ventricle. Exactly every other ventricular contraction is followed by a radial pulse. The radial pulse rate is therefore exactly one-half of the ventricular rate. The apex tracing shows a small "A" wave due to the contraction of the left auricle. The jugular pulse is of the positive type; that is, the wave is systolic in time, although in places a faint presystolic ("a") wave can be made out. This was evidently the result of tricuspid insufficiency. Note the "V" waves. It also shows waves which correspond with the ventricular extrasystoles, which do not reach the radial artery, *i. e.*, produced by the right ventricle. This patient had been taking variable but moderate doses of digitalis in the form of the tincture for three weeks. Two weeks before the pulse tracing was taken the radial pulse had dropped quite suddenly from 92 to 54-48 per minute. One year later the patient was again admitted to the hospital with broken compensation: Edema, cyanosis, ascites, etc., with an enlarged and pulsating liver.[1]

[1] In the first instance the patient was under the care of Dr. H. S. Anders. During her second admission under Dr. Joseph Sailer.

Case III.—Miss J. P. M. (Patient of Dr. J. A. Scott.)

Chief Complaint. Palpitation and epigastric distress after exertion.

Personal History. Chorea at the age of nine years. Severe rheumatic fever three years later. She is known to have had "heart trouble" ever since that time. She has led quite an active life, however, and has rarely been incapacitated. Six years ago she met with an accident—shock and immersion in water—and has never felt quite as well since. She has had three previous attacks similar to the present one—three, two, and one year ago respectively.

Physical Examination. Dyspnea, cyanosis, slight edema.

Heart. A distinct presystolic thrill. Apex in the fifth interspace, 14 cm. from midsternal line. A mitral systolic murmur is noted. The pulse is irregular; rate, 110; temperature, 98°; respirations, 36.

The liver is enlarged. The urine contains a trace of albumin.

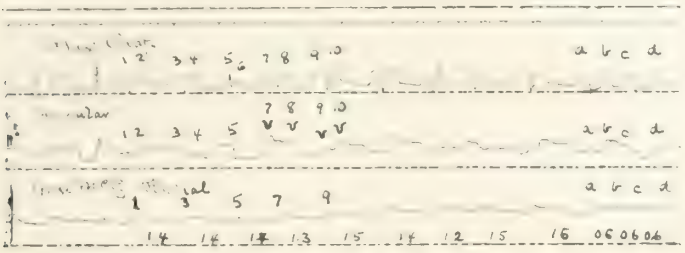
The patient received varying doses, and different preparations of digitalis for twelve days, at which time the pulse rate was 72. On the fifteenth day of the treatment the pulse dropped to 44 per minute, the pulse rate over the precordium was 88. About this time a pulse tracing was taken. It showed a typical bigeminal action, of which only every other ventricular contraction was followed by a radial pulse. The jugular pulse showed a very small auricular (A) wave, the identity of which was almost lost in the large early wave which followed it, showing that the right auricle had contracted very feebly, and that we were dealing with an insufficient tricuspid valve.

Case IV.—(Patient of Dr. J. A. Scott.) E. S., female, aged about forty-five years.

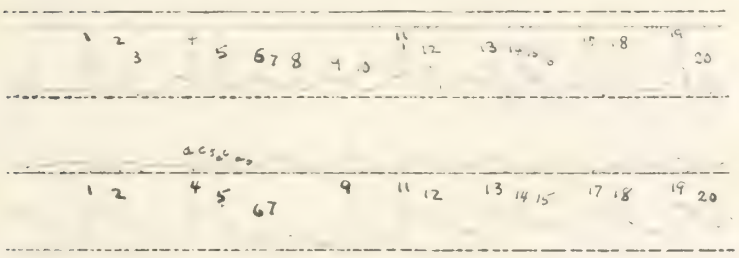
Chief Complaint. Dyspnea on exertion, with occasional vertigo, for the last five months. Three days ago the patient had a syncopal attack, and has been mentally confused ever since. No cough.

Physical Examination. The radial pulse rate varies from 30 to 52 per minute; many beats apparently do not reach the

wrist. The pulmonic second sound is accentuated. There are no definite murmurs, although sometimes a suggestion of a presystolic murmur can be heard.



TRACING XV

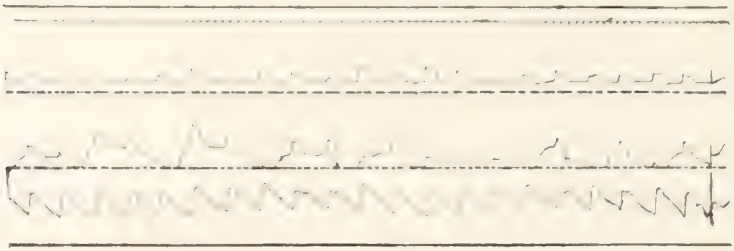


TRACING XVI

Tracing XVI was made on the following day. From an examination of the sphygmogram it is plainly evident that we have to deal here with a case of extrasystolic arrhythmia. The jugular tracing is not very satisfactory, but, so far as one is able to judge, the extrasystoles arise in the auriculoventricular node. The auricle preserves its rhythm during the irregular periods, as shown by the "a" waves in the apex tracing. Ventricular systoles Nos. 3, 8, 10, 16 do not reach the radial artery.

Tracing XVII was taken ten days later and shows the beneficial effect of rest in bed, with fourth hourly doses of strychnine sulphate, gr. $\frac{1}{60}$; tr. digitalis, ηv; and atropine sulphate, gr. $\frac{1}{150}$. The rhythm is now regular, the extrasystoles have disappeared, and the general condition of the patient is greatly improved.

In Cases II, III, and IV we have evidently been dealing with dilated hearts (depression of tone) and with insufficient tricuspid valves. Cases II and III were clearly the results of rheumatic valvular lesions. In Case IV the notes regarding the past history were incomplete. In Cases II and III digitalis evidently caused the bigeminal heart action. In Case IV we had to deal with irregularly occurring extrasystoles, which the administration of digitalis caused entirely to disappear. In this instance there was no pronounced bigeminism, and the whole character of the tracing is quite different from the first three cases. It is certainly



TRACING XVII

an important and interesting fact that under certain conditions digitalis will precipitate an arrhythmia extrasystolic in character, and that in others it will cause the entire disappearance of an apparently similar variety of cardiac irregularity.

We can indorse Mackenzie's statement that "the appearance of coupled beats is at once a signal to lessen the dose of digitalis. No good is to be obtained by pushing it farther, and when one can just manage to keep the patient at the stage where this tendency occurs the best results from digitalis will be obtained—the patient feels easier, makes more urine, and the dropsy is kept under control."

To summarize, then, we find that extrasystolic arrhythmia may simulate heart block by the fact (1) *that the peripheral pulse may be very slow;* (2) *that the jugular veins may be distended and pulsate markedly in the interval between the radial pulses;* (3) *that a muffled third, muscular sound may be heard on auscultation over the heart*

which does not correspond to a peripheral pulse; (4) *that there are no distinctive symptoms of true heart block.*[1] In the vast majority of cases there is, of course, no difficulty in making a differential diagnosis even without sphygmographic tracings. For instance, in the average case of bigeminism the third sound follows closely upon the second, and when one listens carefully one can detect an occasional slight succeeding valvular sound, or one can feel a faint arterial pulse; neither of which conditions is apt to occur in heart block. In cases in which the extrasystoles, instead of occurring regularly and early, appear only occasionally, they are generally followed by compensatory pauses since most of them are ventricular in origin -in these there is still less chance for confusion, since in heart block the arterial pulse rate is generally very regular and the rhythm which one meets with as a result of compensatory pauses is quite unknown. The practical importance of a correct differentiation lies, for instance, in the fact that in many cases of failing compensation with extrasystolic arrhythmia digitalis is the drug par excellence, whereas it is absolutely contra-indicated in heart block due to depression of conductivity.

The fact that in Case I we have seen extrasystoles indicates an increased irritability of cardiac muscle. The occurrence of an occasional prolongation of the a-c interval proves that conductivity was depressed. The appearance of a well-marked pulsus alternans -every other wave small and late —shows that contractility was impaired. There is nothing at all unreasonable in the fact that the different functions of the heart muscle should be thus variously affected. It is quite beyond dispute that they may and do vary independently of each other. Furthermore, in recent experiments on dogs with aconitine, Cushny found a not unsimilar combination of functional abnormalities, *i. e.*, increased irritability with depression of contractility and conductivity. Likewise,

[1] Bachmann has shown that heart block with complete auriculoventricular dissociation may occur without either syncopal or epileptic attacks (American Journal of the Medical Sciences, March, 1909). Mackenzie, on the other hand, has reported cases of nodal rhythm which presented the symptoms of the Adams-Stokes syndrome (Heart, 1909, i, 36).

some cases published by Mackenzie have shown that increased irritability may even exist hand in hand with diminished conductivity. During the first part of the time that our case was studied we observed only extrasystoles or bigeminus. During the latter part pulsus alternans was generally present. This increasing weakness of the power of contractility foreshowed the approach of a lethal termination. We were not surprised, therefore, to find, on returning to the city at the end of the summer that the patient had died some two months after his admission to the Pennsylvania Hospital. During this time the patient had numerous, chiefly nocturnal, attacks of dyspnœa, which were relieved by morphine, atropine, or amyl nitrite. Gradually he developed edema, and finally, following apparently upon an attack of cystitis due to the B. coli communis, the patient died in coma from a general infection.[1]

AUTOPSY NOTES (DR. DRAPER).

The heart weighs 490 gm.; it is large, flabby, and yellowish purple in color. Over nearly the whole right ventricle there is a wrinkled, yellowish thickening of the pericardium. The surface of the heart elsewhere shows a very fine stippled yellow and red appearance, resulting from dilated capillaries upon a yellowish (jaundice) background. The right auricle and ventricle are greatly dilated. The auriculoventricular ring measures 14 cm. The endocardium is smooth and glistening, the valves are soft and delicate. The mitral leaflets are slightly thickened and retracted at their margins. The aorta and the coronary arteries show fine yellowish thickenings. The left ventricle measures 2.5 cm.; the right ventricle, 1.5 cm. The muscle shows yellowish fleckings through the endocardium, in places a typical tiger-skin appearance. On cross-section the muscle shows many yellowish mottlings and fine grayish striations.

[1] I am indebted to Dr. Morris J. Lewis for the notes of the case while in the Pennsylvania Hospital, and to Dr. Draper for the autopsy records.

Microscopically, the muscle fibers stain poorly and do not show cross-striation. There is a moderate increase of interstitial tissue and some infiltration of fat, especially in the right ventricle.

Anatomical Diagnosis. Chronic pericarditis. Chronic interstitial myocarditis and fatty degeneration of the heart muscle. Endarteritis deformans. Chronic interstitial nephritis and hydronephrosis. Chronic perihepatitis and hepatic cirrhosis. Chronic passive congestion of the lungs, liver, and spleen, etc.

DISCUSSION

Dr. John B. Roberts: I have been interested in watching the intermission of the pulse beat in a couple of boys who have had measles. I am not now familiar with measles as a clinical disease, but this intermittent pulse in one case was present for about a year and a half after the attack and finally disappeared. My explanation was that there was a mild myocarditis. During this whole summer I have had an opportunity to examine a young boy who after measles had an intermittent pulse. At the time of the intermission of the pulse I have noticed, with my ear to the chest, the extra beat of the heart, suggesting the motion of a fish lying in the bottom of a boat. This, I suppose, was the extra systole. The boy seems to be better under belladonna than under digitalis. He now has a pulse more regular, with fewer intermissions. The whole question ought to be as interesting to us who are studying these questions clinically as well as to those who are physiologists. The boy seems to be doing better under belladonna than he did under digitalis, although the improvement may be due to the fact that he is regaining the general tone of the muscle and that the irritability is subsiding under the increased time rather than from the belladonna.

Dr. A. A. Eshner: When I first saw this man at the hospital he seemed to present the picture of myocarditis and arteriosclerosis, of which we see so many instances at the Philadelphia Hospital. His heart was rapid, but I do not recall whether it was rhythmic or not. There was no suggestion of heart block at this time. There was no cyanosis, no syncope, no convulsion. While under observation, as Dr. Norris has related, the pulse became much less frequent. The frequency became reduced to one-half, and at this time one could hear the third sound that Dr. Norris has described, in addition to the muscular first sound and the valvular second sound. Dr. Norris made sphygmographic and sphygmomanometric examinations, and these seemed to show that the case was one of heart block. Further observation, however, disproved this conception of the case, and, as Dr. Norris has related, we came to the conclusion that the condition was one of myocarditis, and this has since

been verified by the postmortem examination. The case itself emphasizes a view that had been in my mind previously, based upon clinical observations and graphic and sphygmomanometric records, namely, that there is a relation between the varied forms of myocardial degeneration that for convenience sake we classify clinically as myocarditis and the condition of heart block. It seems to me that degeneration of the heart muscle, whether fibroid or gummatous, not necessarily involving the auriculoventricular conducting bundle of His, may cause derangement in conductivity or contractility, or in the other attributes of the muscular wall of the heart, and give rise to disorders of rhythm that we include under the general designation of arrhythmia, and of which heart block must be considered as an extreme type. Dr. Norris seems inclined to attribute many of the circulatory variations, particularly the failure of the pulse at the wrist, to increased blood pressure. I should imagine that that were but one factor in the determination of the manifestations, and that the underlying factor was the state of the myocardium and that by reason of its inefficiency it was unable to compensate for the increased burden thrown upon the heart by reason of the increased blood pressure.

Dr. William Pepper: It is a treat to anyone who has dabbled in this subject to hear a paper that has been worked up as fully as this one has been. One point which interests me is the lack of our ability to feel these small extrasystoles. The finger is much less sensitive than the instruments in detecting extrasystoles, but at times, as shown in this case and as has been seen in others, even with the finer instruments, one cannot perceive them at the wrist or in the brachial artery. It has been thought that in some of these cases the aortic valves were not opened by the ventricular beat, and that therefore no blood comes through and thus no tracing is obtained of them from the radial or brachial. It is rather fortunate that frequently these very small beats, which, though hard to detect at the wrist, are very easily detected at the apex, the heart being more or less empty, so that when it does contract it gives a kind of flap or slap, and often gives in the cardiogram a good-sized curve. I do not say that we are able to tell whether in the small beats the valves open or not, but I think that when we are unable to detect, by instrumental means, any wave in the peripheral arteries, that then probably the aortic valves have not opened.

Dr. S. Solis Cohen: I should like to ask Dr. Norris in continuing, according to his announced intention, to test in various ways what has been well termed by a previous speaker the reserve force of the heart, to include the effect of local applications of heat and cold over the precordium. Clinically, simply by estimating the rhythm and force of the pulse with the finger, also in some cases with the sphygmograph and the sphygmomanometer—but for practising physicians it is more readily done with the finger—I find that when a heart responds well to a momentary application of heat, followed by cold, the prognosis is rather good. When this application increases the

arrhythmia the prognosis is bad. It is a rough but quite a ready way of getting at the amount of good cardiac muscle remaining to respond to medicinal and hygienic measures.

Dr. Robert N. Willson: I wish to speak of an interesting animal observation which I stumbled upon quite recently by accident. I think that it not only excites interest in this connection, but tends to confuse one after he has apparently and finally straightened out the interrelation of the ventricular and auricular systoles. In studying certain problems in tuberculosis of the guinea-pig I noticed upon taking out the heart that when it was exposed to the air the pulsation, which almost immediately after removal of the heart from the pig assumed the character of a fibrillary tremor, again changed its nature. The ventricular contractions stopped almost completely, and the auricular systoles continued their rhythm. Then the auricular contractions seemed to cease and the ventricular resumed and later again discontinued. Then for a time and occasionally both were synchronous. Finally, before the contractions stopped altogether the ventricular systoles gradually decreased in power and extent and the contractions seemed to recede toward the auricle, then toward the great sinus, and then disappear. If these phenomena are produced in any such way in the human body in disease, it must needs be that very trifling alterations in the conditions of the body, chemical changes, etc., assume great importance in alteration of the normal beat. This would account for many of the conditions which we now try to explain along chemical lines. I feel that a great deal that has recently seemed clear is still obscure; and that a great deal that is written about the significance of the auricular and ventricular contractions is by no means thoroughly explained, still less understood. It is my belief that when we have gotten to the bottom of the difficulty it will be along different lines than that suggested tonight. I want to congratulate Dr. Norris upon the thoroughness with which he has worked this matter out, but I must confess that it does not explain what I see in the contractions in the guinea-pig's heart. If the human heart acts as does the guinea-pig's then I think the conditions in disease are not understood. We know simply that dissociation of the auricles and ventricles is possible. The causal factors and the governing laws still remain obscure.

Dr. W. T. Longcope: I should like to ask Dr. Norris whether any experiments have been made upon animals with a view to producing extrasystoles by increasing the blood pressure? I was under the impression that cardiac arrhythmia due to extrasystoles had been brought about in dogs by compression of the aorta.

Dr. Norris, closing: In answer to Dr. Longcope's question, it has been repeatedly shown that partial ligation of the aorta in animals will produce extrasystoles. There is absolutely no doubt that increased pressure within the heart itself is one of the causes of extrasystole.

As to Dr. Roberts' query and his report of the cases, I would say that it is quite common to find arrhythmias appearing in young children, particularly after febrile attacks of various kinds, not only in measles but in all sorts of infections where there has been fever. This juvenile or infantile type of arrhythmia is better designated as sinus arrhythmia. It is probably due to overaction of the vagus nerve affecting the sinus rhythm. Therefore, when you give belladonna which depresses the vagus nerve the arrhythmia disappears. That is the generally accepted explanation, and I think it would apply to the cases mentioned by Dr. Roberts. Sinus arrhythmia is entirely associated with respiration. Under normal circumstances the pulse rate will go up during forced inspiration. Under pathological conditions normal inspiration and expiration will produce a change in the pulse rate. This is termed sinus arrhythmia.

In answer to Dr. Willson: I did not mean to indicate that we had cleared up this whole question by any means. No one can fail to be impressed with the fact that there are numerous gaps. I do feel, however, that although we may have to correct, and perhaps change entirely, some of the views which we now hold, yet taking the matter up in this way on the basis of the myogenic theory, and considering the five functions of the heart muscle independently, has given us a working basis on which to theorize, just as Ehrich's hypothesis of the blood complement has furnished the bacteriologist with a working basis.

Dr. Eshner in his remarks about blood pressure said what I intended to convey—that mere increase of blood pressure in the normal heart, unless very extreme, would not bring about such results as we have seen. But in a diseased heart such increase of pressure as followed the use of digitalis, deep breathing, and abdominal compression did call forth extrasystoles.

EXOPHTHALMIC GOITRE.[1]

By JAMES TYSON, M.D., and JOSEPH SAILER, M.D.

The serum treatment of exophthalmic goitre is still in the experimental stage. Somewhat contradictory results have been obtained by the different observers, and it is not clear from our present knowledge of the subject just why this should be. There are three possible explanations:

1. That exophthalmic goitre is rather a syndrome than a disease entity. It is easily conceivable that more than one cause may produce the group of symptoms, or at least some of them, in different cases. Indeed, there are still physicians who believe that the cervical sympathetic is the chief offender and who practice its resection as a therapeutic measure, and even Kocher at one time, with all his experience, was inclined to locate the causative lesion in the medulla oblongata.

2. The serum may vary very greatly in its antitoxic content. There is every reason to believe that this is so, and indeed, it was observed by Drs. Roger and Beebe when they began their experimental work.

3. The method of administration may be at fault in the unfavorable cases. As it is comparatively simple, there seems to be no good reason for believing that it is of much importance.

The treatment is, of course, based upon a theory for which there is much evidence, that exophthalmic goitre is due to excessive activity of the thyroid gland and the intoxication of the organism with its normal or moderately abnormal internal secretion. Upon

[1] Read November 3, 1909.

the assumption that the diseased gland contains an excessive amount of secretion, fragments of the gland are introduced into animals until they acquire a distinct toleration to it. This toleration is supposed to be brought about by the formation of some antitoxic or antidotal body in the blood serum, and this serum, therefore, should counteract the effect of the toxin in the person affected by the disease. It is, of course, an interesting fact that rarely does such an antitoxin develop in the patient's serum, although, if the theory were true, there is reason to believe that at least a certain proportion of cases would exhibit spontaneous recovery. Cases, of course, do get well without surgical intervention, but complete recovery is comparatively rare and relapses are frequent. The cases we report are typical. The treatment was carried on with serum furnished by Dr. Beebe, and he was frequently consulted regarding the further progress of the treatment, and was sufficiently interested to visit one of the patients in the wards of the hospital. We desire here to express to him our thanks for his generosity in furnishing the serum and our appreciation of the altruistic and scientific spirit manifested in the whole course of his investigations, not only upon this, but upon all other subjects that he has undertaken.

Case I.—Mrs. M. B., aged twenty-three years; white. Admitted to Dr. Tyson's service at the University Hospital, October 1, 1908, complaining of nervous feelings, disturbed vision, palpitation, and swelling of the neck.

Previous History. About one year ago it was noticed that her eyes were becoming more prominent. Six months ago she discovered a swelling in the neck, which has since increased in size. Three months ago she became very nervous, her hands shaking, and there was much palpitation of the heart. About the same time she had difficulty in seeing, and objects would become blurred or appear double. Her appetite was good, the bowels regular, and she was sleeping well.

Family History. One sister out of eight brothers and sisters now living has goitre; otherwise it is negative. The patient is a native of Pennsylvania; she has one child, which is living and well. There have been no miscarriages. Menstruation is normal. On admission it was noted that she was pale and poorly nourished. The eyes were extremely prominent, and Stellwag's and von Graefe's signs were present. The pupils were normal. There was a slight tremor of the tongue and marked tremor of both hands. The right lobe

of the thyroid gland was greatly enlarged and pulsated visibly, and over it there was a distinct thrill and loud bruit. The left lobe was less enlarged. The circumference of the neck was 13 inches. The lungs were normal. There was vigorous pulsation over the whole precordium and a wave-like contraction of the ventricles could be seen. The impulse was in the fifth interspace to the left of the midclavicular line. The area of absolute cardiac dulness extended from the third rib downward, and from midsternum to half an inch to the left of the midclavicular line. The heart sounds were clear; over the pulmonary cartilage and over the third costal cartilage to the left a loud systolic murmur could be heard. The abdomen was normal. The urine was normal. The red blood cells were 5,100,000, the white cells blood 14,000; hemoglobin, 74 per cent. The pulse rate ranged from 90 to 130. The respiratory rate, from 20 to 30. The temperature was normal throughout her stay in the hospital, with the exception of a slight transient infection. The patient was put to bed and given potassium bromide and tincture of digitalis. On October 18 she was given her first injection of thyroid antitoxin serum. This was continued daily for three days. On the 24th the injections were given every other day until November 10. During this time condition remained about the same. Her appetite became poor, and on several occasions she vomited. On the ninth, in view of the absence of definite results, she was given a detoxicated thyroid tablet four times a day. This was continued until November 19, when the serum treatment was interrupted. On November 12 it was noted that the eyes were prominent and the lids wide, showing sclera above and below. Winking was infrequent. There was a positive von Graefe's sign, but no pulsation of the eyeballs. All the lobes of the thyroid were moderately enlarged, and they all pulsated. There was a thrill over them and also over both subclavians on slight pressure. The cardiac dulness had increased, extending from third rib downward, and from right border of sternum to left anterior axillary line. The apex beat was in the fifth interspace on left anterior axillary line. It was diffuse, and there was a moderately powerful systolic thrill. Over the base of the heart a strong systolic impulse and a systolic thrill and a diastolic shock could be felt. The heart sounds were clear, the second pulmonic sound was accentuated. A systolic murmur could be heard over the entire precordium, and was loudest at the pulmonic area. There was a loud, continuous bruit, with systolic intensification, over the carotids and thyroid gland. The lungs were normal. The right kidney was in the first position. Otherwise the abdomen was normal. There was a marked tremor of the hands. The blood count showed: red blood cells, 4,130,000; white blood cells, 10,900; hemoglobin, 60 per cent. On November 20 the patient was given 10 grs. of citric acid three times a day. Under this treatment there was no apparent change in her condition, and on the 27th Dr. Beebe saw her and advised the injection of 10 mm. of serum every third day. This was commenced on December 2, and continued until January 18. There was a

slight increase in weight, but otherwise the patient's condition remained the same. On the 18th she was discharged practically in the same condition as when she entered. The only immediate effect of the injections that was observed consisted of a slight acceleration of the respiratory rate, and this was transient.

Case II.—Mrs. H. T., aged twenty-eight years, was admitted to Dr. Sailer's service at the Presbyterian Hospital on January 18, 1909. She complained of palpitation of the heart, shortness of breath, weakness, nervous feelings, and shooting pains in the arms. Two months before admission her child died, and she had been overcome with grief. She had the symptoms of a bad cold, was very weak, and thought she had rheumatism. Upon further questioning, it was elicited that she had palpitation and nervous spells four years ago, immediately after the death of her husband. Two years later, enlargement of the neck was first noticed. She had had typhoid fever and pneumonia at the age of seventeen years. She has always taken cold easily. She was married at the age of eighteen years and had borne two children. Menstruation began at the age of ten and one-half years, and has always been normal. Patient was poorly nourished and pale. Her eyes were remarkably large and prominent, the palpebral fissures were wide, and there was a positive von Graefe's sign. Winking was infrequent. The pupils were normal. The mucous membranes were pale. The tongue was tremulous. The thyroid gland was greatly enlarged, especially the right lobe and the isthmus, and pulsated distinctly. There was a fine continuous thrill in both lobes, with a systolic exacerbation. There was apparently a positive pulse in both external jugular veins. The peripheral arteries were soft. The pulse was rhythmical and slightly receding. The apex beat was in the fifth interspace at the anterior axillary line. It was one inch broad, and there was a strong systolic impulse and a faint diastolic shock. A diastolic shock was also felt at the base. There were no thrills. The cardiac dulness extended from fourth rib downward, and from the left border of sternum to the left midclavicular line. At the apex there was a loud first sound, a soft blowing systolic murmur and a loud second sound. At the pulmonic cartilage a faint first sound, a soft, faint systolic murmur and a very loud second sound. At the xiphoid a sharp first and a moderate second sound, but no murmur. The lungs were normal. There was a loud bruit over the thyroid gland, with a systolic exacerbation. The abdomen was retracted in the upper segment, slightly convex in the lower segment. There was a positive Stiller's sign on both sides and moderate separation of the recti muscles. The lower border of the liver was at the level of the umbilicus. The right kidney was in the second position, the left kidney in the first position. The lower border of gastric tympany extended to a line below the left anterior superior spine of the ilium. There was no splash three hours after taking food. The pulse of the main arterial trunks of the

abdomen could be easily felt. There was a loud systolic note over the large peripheral arteries, and murmurs could easily be produced in all the peripheral and abdominal arteries by pressure. There was a distinct constant tremor of the hands. The tendon reflexes were normal. On admission, the patient's weight was 102 pounds. The first serum injections were given on February 16, 17, and 18. These were followed by a violent reaction, the temperature rising to 102.5°, and the pulse increased from about 100 to 120. The injections were then given on the 20th, 22d, and 24th. After the injection on the 22d the temperature returned to normal, and there was no subsequent reaction. The serum was then given on February 27, and on March 2. During this time the patient's weight rapidly decreased, reaching 84½ pounds on March 2. There was complete anorexia, occasional vomiting, and excessive weakness, so that on one occasion when she attempted to get out of bed she fell to the floor. The circumference of the neck remained constant at about 12½ inches. There was no improvement in the tachycardia, the tremor of the hands, or the appearance of the eyes. The patient was excessively emotional, and had frequent attacks of weeping. The urine contained constantly a faint trace of albumin and on one occasion a few casts were found. The blood count of January 20 was: red blood cells, 4,690,000; leukocytes, 6800; hemoglobin, 85 per cent. On February 20, during the reaction from the serum, the leukocytes were 14,800. After this they remained between 4600 and 5800. The systolic blood pressure remained nearly constant at 130. When the patient was first admitted she was given 20 grains of citric acid three times a day. This had no appreciable effect. After the serum was discontinued she was given hydrobromate of quinine. Her appetite improved somewhat and she seemed to be a little stronger, but there was no appreciable gain in weight. She was discharged in about the same condition as when she entered the hospital. Subsequently she reported by letter that she still felt a little stronger, but otherwise was the same. This patient was advised to have an operation, but declined.

Case III.—Miss A. B. K., aged twenty-six years. Admitted to Dr. Sailer's service at the Presbyterian Hospital on January 23, 1909, complaining of shaking, nervous spells, made worse by excitement; of excessive perspiration; of constant nausea, and of excessive appetite. She had suffered with amenorrhea for six months. She stated that for many years she has had palpitation of the heart. For the past two or three years she has had attacks of nausea and vomiting. For a long time she has been unable to satisfy her appetite, and taking food improves the nausea. She craves particularly for salt. The present illness began in June, 1908, after an emotional shock. Menstruation ceased at this time, and since then she has had warm flushes and perspires easily upon exertion. The family history was negative. During childhood she had scarlet fever and pneumonia. At the age of seventeen years there was some kidney trouble. At the age of twenty-one years she had

typhoid fever. She has noticed an occasional swelling of the feet, and, at long intervals, pain in the cardiac region. She is inclined to have severe nervous attacks if emotionally excited. Menstruation began at twelve years, and at first was very irregular, and then was quite regular until it ceased. She states that the enlargement of the thyroid began at the age of eleven years, and she thinks she has kept it reduced in size by massage. During the grief and depression from which she suffered last summer it grew rapidly worse, and now occasionally produces a choking sensation. Tight clothing causes her to get red in the face and very short of breath, and these symptoms are always increased by the presence of strangers.

Physical Examination. The eyes were not abnormally prominent. There is a distinct von Graefe's sign. The pupils were normal. The right lobe of the thyroid was distinctly enlarged, and there was expansile pulsation in the neck. A distinct thrill could be felt over the thyroid gland. The pulse ranged from 82 to 100. The arteries were soft. There was a heaving systolic impulse over the whole precordium. The apex beat was in the fifth interspace, just outside of the midclavicular line. The area of absolute cardiac dulness extended from the third rib downward, and from the right border of the sternum to the midclavicular line. The heart sounds were loud and clear. The pulmonic second sound was slightly accentuated. Over the heart a loud systolic murmur could be heard, and was most distinct at the pulmonary orifice. There was a continuous bruit, with systolic exacerbation over the thyroid gland. The lungs were normal. There was a fine tremor of both hands, more pronounced when the fingers were extended. The abdomen was normal. The patient's general nutrition was very good. The urine on one occasion contained a trace of albumin and some pus; otherwise it was normal. The leukocytes varied between 5200 and 7000. The red blood cells were not counted. On one occasion the patient complained of double vision, but Dr. William T. Shoemaker, who examined the eyes at this time, could find no disturbance of the ocular muscles. During her stay in the hospital she had frequent attacks of violent weeping, sometimes lasting for hours, for which she could give no explanation, and during which she was apparently not more excited or disturbed than at other times. Her condition during her stay in the hospital showed very little change and she was discharged on March 26, in about the same condition as that in which she entered. On admission her weight was 140 pounds. She was placed on citric acid, 20 grains, three times daily, which was continued until February 16. Serum was started on this date and given daily for three days—on alternate days for three injections and every third day for three injections. After the ninth injection there was a sharp attack of fever, reaching 103°. No cause could be found for this, nor was there leukocytosis, but it lasted for two days and terminated by crisis. During her stay in the hospital her weight decreased from 140 pounds, on admission, to 133 pounds on February 15. On March 3

it was 134½ pounds, and then rapidly decreased to 122½ pounds on March 29. The injections of serum were stopped on March 8 and recommenced at four-day intervals on the 17th. Then, on the 29th, their frequency was increased to every other day. Her weight fluctuated somewhat, but on the whole was lower, and on May 2, at the time of her discharge, she weighed 119½ pounds. On April 22 she was given hydrobromate of quinine, and this was continued until she left the hospital. She reported some months after leaving the hospital that she was somewhat better.

The citric acid was given to all three of these patients upon the theory of one of us that it might serve in some way to counteract the poison of the thyroid gland. McCallum has shown that in the tetany of cachexia thyreapriva the calcium salts may relieve the symptoms. There is some reason to believe that, so far as the coagulation of the blood is concerned, citric acid is the physiological antithesis of the calcium salt, and it was supposed, therefore, that it might also antagonize the poison produced by the excessive action of the thyroid gland, if the calcium salts antagonize thyroid insufficiency. It was used in one case of very chronic exophthalmic goitre in a man aged forty-five years, and followed by the most extraordinary results, that is, very rapid increase in weight, with alleviation but not cure, of the nervous symptoms. In a second case, a man, seen in consultation with Dr. McDowell, a cure was reported. In a third case, a woman, there was a gain in weight and slight relief of the symptoms. In a fourth, of severe exophthalmic goitre, and in two other cases of very slight exophthalmic goitre, no improvement was noted, nor was any improvement noted in the three cases here reported.

The serum treatment, although given as carefully as possible, was a complete failure. In one case, the second, it apparently caused a violent reaction, that, however, seemed to do no particular harm. None of the cases, however, showed even a temporary improvement in their symptoms, and all of them steadily lost weight. Dr. Beebe furnished several supplies of serum during the course of the treatment, obtained, we believe, from different animals immunized with different glands, so that it is hardly likely that all the samples that were employed were inert. It seems

more probable that for some reason these patients were refractory to the serum, and this suggests that there are different types of the disease. Unfortunately, exophthalmic goitre is one of those conditions in which it is difficult to estimate what part suggestion may play in the improvement of the symptoms, so that there is always this incalculable factor in every case of partial improvement. This must exist quite as much for other methods of treatment, such as thyroidectin, which appears to have fallen completely out of favor, and possibly the feeding of the patients with milk of goats whose thyroids have been removed. At present, however, we are obliged to conclude that surgical removal of the gland is the only efficient remedy at our command.

DISCUSSION.

Dr. John B. Deaver: My experience with Beebe's serum in exophthalmic goitre leads me to believe that it is of no use at all. I have tried it in a number of cases to bring up the leukocytes, but have had no benefit. I usually operate because operation practically cures all cases.

Dr. S. Solis Cohen: I would take exception to Dr. Sailer's remark that, as a rule, cases of Graves' disease do not recover without operation (if I correctly understood his statement). My experience with this syndrome is not inconsiderable, and I am satisfied that a vast majority—somewhere between 60 and 75 per cent.—of all cases get well without any special treatment, except rest and hygienic management, provided they are recognized early. I speak in approximations, of course, not in exact figures. Another large portion, say 20 or 25 per cent., will get well if we add to the hygienic management appropriate medicinal treatment. This leaves a possible 5 to 8, or at most 10 per cent. of intractable cases for surgery. It has not been my own fortune to meet with that 5 per cent. as yet, but such cases necessarily form nearly 100 per cent. of those that come under the observation of surgeons. The experience of Kocher, or of the Mayos, or of our friend Dr. Deaver, is therefore not to be applied to early cases or to all cases. It will be gathered that I believe the syndrome to be much more common than is generally recognized; and also, that in speaking of spontaneous recovery I do not include advanced cases such as those reported tonight. I have, however, in reporting the results of treatment in cases of Graves' disease always been careful to recognize and point out the possibility of error, namely, of attributing to the special therapeutic measures employed in the individual case a recovery that might have been independent of the treatment.

The action of Beebe's serum is extremely interesting. Through the kindness of Dr. Beebe I had the opportunity to try it in three cases. In one of these it was without result; it was neither harmful nor helpful. In a second case it was distinctly helpful. The patient, who was sent to me from the country, had a very large goitre, had been ill for a long time, and was admitted to the Jefferson Hospital in a rather desperate condition. The heart was feeble, much dilated, with mitral, and possibly aortic, regurgitation; there was orthopnea and dropsy; and the patient was almost in collapse upon entering the hospital. Of course, immediate surgery was out of the question. We nursed her for a while, treating the heart with digitalis and strophanthus, etc., and there was temporary improvement in symptoms; but my surgical colleague decided that the prospect of death from ether and shock was too great to permit thyroidectomy to be considered. Dr. Beebe had furnished me with serum, but I had had no experience with its use. I had heard of bad results therefrom; I knew that the patient might die with or without it at any minute; and I did not wish the death to be attributed to malpractice. The gravity of the prognosis and the uncertainty of the effect of the serum were, therefore, explained to the husband and, at his request, to the patient. Both gave consent to the injection. Within an incredibly short time, incredibly great symptomatic improvement was manifest. The goitre and the exophthalmos were slightly diminished, but the most astonishing relief was to the secondary cardiac symptoms. The dropsy disappeared, and for the first time in years the patient slept through the night without an attack of orthopnea. In the course of a month we were able to send her home. Unfortunately, the subjective relief was so much greater than the improvement in physical conditions that she went about her household duties and was again prostrated. The attending physician, at my suggestion, resorted to Beebe's serum again, and the woman for a second time was able to get up and work. She lived, I think, for a year or more after that. Death was the natural result of the cardiac degeneration. Autopsy was not made.

The third case was one of long duration seen at the Philadelphia Hospital, in which the symptoms, while pronounced, were not threatening and in which there was great improvement after the use of the serum. The patient relapsed and returned to the Hospital, and it was thought that as much benefit was then derived from the use of saline injections as previously from Beebe's serum. The psychic element in that case cannot therefore be overlooked. However, the one remarkable observation at Jefferson Hospital convinces me that in some cases, at least, Beebe's serum is of decided value—but I should not use it in early cases.

This brings us to the question of the real nature of Graves' syndrome—a subject too big to discuss here and now. I am of those who believe that the thyroid intoxication, to which unquestionably many distressing symptoms

are owing, is a secondary condition and not the origin of the syndrome. Consequently I find it rational to believe that antithyroid treatment (whether by serum, animal extracts, or surgery) will be of benefit in so far as it combats or prevents thyroid intoxication and the results thereof, but no further. It does not reach the origin of the thyroid tumor, which is the same as that of the syndrome in general. It is inapplicable in the important, formative stage of the disorder.

Dr. J. Norman Henry: Some three years ago I had the opportunity of treating a case of exophthalmic goitre with Beebe's serum with very much the same result as Dr. Sailer has described. The patient was in no way benefited; in fact, at times, the serum seemed to do harm, increasing the nervous symptoms. I gave the serum under the advice of Dr. Rogers and Dr. Beebe from time to time, because of my own inexperience in the method of treatment. In talking with Dr. Rogers about the case afterward, he told me that he thought a certain class of cases of exophthalmic goitre were particularly benefited by the serum, namely, the acute toxic form. My own case was of the ordinary chronic type, with small goitre, a moderate degree of exophthalmos, and marked nervous symptoms. I have been somewhat discouraged in its use in my very limited experience, but hope for better results in other classes of cases. In the more chronic forms of the disease I am not hopeful of the treatment being of any particular benefit.

Dr. Alfred Gordon: Sufficient material has accumulated to prove that exophthalmic goitre is not due to hyperthyroidization. I agree with Dr. Cohen that changes in the thyroid gland are a secondary condition. There are many arguments in favor of the latter opinion. How can you explain cases of exophthalmic goitre, without a goitre, on the basis of hyperthyroidization? How can you explain the occurrence of a unilateral group of symptoms of exophthalmic goitre if the disease is due to a thyroid toxemia? Why should it affect the upper part of the sympathetic system, which innervates the thyroid and carotid arteries, and not the lower part, which supplies the abdominal aorta?

On the other hand, exophthalmic goitre has been observed in association with ptosis of viscera. Brissaud reports a case of floating kidney with exophthalmic goitre in which a suitable belt removed the latter condition. Nasal polyps associated with Graves' disease have been observed; when the former were removed the exophthalmic goitre disappeared. Tillaux performed successfully a thyroidectomy, and four years later symptoms of exophthalmic goitre developed.

For all these reasons, and especially for anatomical reasons, it is hardly possible to accept the hyperthyroidization theory. In a majority of cases that have come to autopsy hemorrhages have been found in the medulla. Only very recently a case was reported in *Deutsche Zeitschrift fur Neurologie*,

No. 25, in which a woman died of exophthalmic goitre and hemorrhages were found in the medulla over the entire floor of the fourth ventricle. Experimental researches also tend to prove that the nervous system is at the bottom of the trouble. Filehner in 1879, later Bienfait, Durdufi, have demonstrated it experimentally. On the other hand, Soupault overfed animals with thyroid and failed to produce Graves' disease. Whether the medulla alone or the sympathetic system through the medulla is the cause is difficult to tell, but changes in the medulla have been found everywhere.

Dr. Deaver made a somewhat sweeping remark that only surgeons can cure exophthalmic goitre. I can join Dr. Cohen in citing a few cases under my care in which medical treatment improved considerably exophthalmic goitre.

Several years ago I made a comparative statistical study of the surgical results obtained from various methods, and I have seen that operations on the sympathetic system give better results in the majority of cases than thyroidectomy. Jonnesco especially reports a number of operations on the cervical sympathetic nerve which have given him better results than complete thyroidectomy. In conclusion, I may say that in view of clinical, experimental, and anatomical data, also taking into consideration the operative results, I believe that exophthalmic goitre is a disease of the central nervous system and not due to hyperthyroidization.

Dr. Sailer, closing: In regard to Dr. Deaver's statement, I don't think he interpreted me quite rightly. He went to one extreme, as I believe Dr. Cohen did to the other. I have seen cases of exophthalmic goitre greatly benefited by medical treatment. I cannot say that I have ever seen cases cured. There were always some residual symptoms showing that the disease was in abeyance but latent, and several times I have seen cases in which it recurred. I think Dr. Cohen's experience is exceptional. It is not my own experience or the experience of some who have written on the subject. I am quite sure that so many cases coming to the surgeon is proof that quite a number of physicians fail in their efforts.

I did not go into the etiology of exophthalmic goitre. There are many views and as none of them are capable of definite proof, they are fit subjects for discussion but not for reaching any definite or satisfactory results. These three cases were given rest and they were subjected to all the usual hygienic measures. Naturally, while the serum was being given other drugs were omitted.

CONTROL OF HEMORRHAGE IN TYPHOID FEVER CONSIDERED FROM THE SURGICAL STANDPOINT.[1]

By RICHARD H. HARTE, M.D.

Next to perforation of the bowel, hemorrhage occurring in the course of typhoid fever, has always been considered by physicians as the worst of its many varied and serious complications.

The treatment of this complication has consisted chiefly in quieting the peristaltic action of the bowel, by stopping all food by the mouth, applying ice locally to the abdomen, and by the giving of opium, with astringents and the hemostatics internally. High rectal injections of hot normal salt solution also have been used with apparent good effect.

In a large number of cases this line of treatment has been crowned with success. At least, the bleeding has stopped and the patients ultimately recovered. In others, the bleeding has continued, and, notwithstanding the medication and local treatment, the patients have died from loss of blood. These instances are few as compared with those first mentioned, and it is to these fatal cases, in which death is due directly to hemorrhage, or hemorrhages, that the author wishes to suggest surgical interference.

Physicians, and especially surgeons, who have had the opportunity of seeing the abdomen opened in cases of perforation of the intestine, the perforation located, and closed with sutures or an artificial anus established, followed by ultimate recovery, which undoubtedly would have died had it not been for the surgical

[1] Read December 1, 1909.

interference, cannot, I believe, but think that the same measures are applicable, and should at least be tried, in serious hemorrhagic cases which do not yield to medical treatment.

The definite percentage of deaths directly due to hemorrhage is hard to determine, as the general condition of the patient, virulence of the infection, and the various other complications must be carefully considered before stating whether death was due to all or any particular one of the complications.

At the Pennsylvania Hospital, in Philadelphia, where there are always a number of typhoid cases, it has been noticed that during some epidemics which seemed to be almost of a malignant type, perforation of the bowel was much more common, and hemorrhage from the same source occurred in a much larger percentage of cases.

It has also been shown by statistics from the same institution, prepared by the late Dr. J. Alison Scott, that a large percentage of hemorrhages were followed by perforation.

The frequency of hemorrhage varies in different statistics; Robinson found at the Pennsylvania Hospital that, in the past three years, there were 1548 cases of typhoid fever, of which 132 were fatal. In 31 hemorrhage from the bowel took place, of which number 18 died; 13 of the 18 died directly as the result of hemorrhage, while the remaining 5 died from other causes.

McCrea (Osler's *System*) found in 23,000 cases that 7 per cent. were complicated by hemorrhage. He also found that certain families seemed more prone to this complication than others, and also that it varied greatly in the different epidemics analyzed.

Statistics show, and my own experience of 38 cases of perforation bears out the same conclusion, that the seat of perforation is usually found in the last eighteen inches or two feet of the ileum, and naturally in this locality, where the ulceration is most extensive, will be found in the majority of cases the site of hemorrhage.

Some surgeons advise the opening of the abdomen in the median line, but it has been my custom to make the incision through the outer border of the right rectus, as this incision usually directly overlies the seat of trouble. The incision should be free enough

to allow a speedy examination to be made of the intestine, in order to locate as quickly as possible the condition sought for.

After the abdomen has been opened, the cecum should be found, and, starting from this point, a thorough examination made of the ileum. If perforation and hemorrhage occur together from the same ulcerated area, both may be treated at the same time by a method which will be spoken of later.

Personally, I have operated upon two such cases, the histories of which are as follows:

Case I. J. G., aged thirty-two years; orderly at the Pennsylvania Hospital. On May 18, 1903, he was admitted to the medical wards, and was supposed to be in the eighth day of typhoid fever. He had nausea, vomiting, and pain in the back and abdomen, with marked nervous symptoms. The abdomen was slightly distended and tympanitic, without rigidity. He complained of slight tenderness in the right iliac fossa and below the left costal border.

Two days after admission the abdomen was distended, and while the pain and tenderness were somewhat improved, on May 11, the fourteenth day of the disease, he had a profuse diarrhœa, and blood clots were present in the stools, with some abdominal distention.

The following day, and in fact until May 17, the twentieth day of the disease, he continued to pour blood into the bowel. The pulse was weak and almost imperceptible at the wrist. I saw him in consultation with Dr. Lewis, and we decided to open the abdomen and see if we could find the bleeding point in the intestine. At that time, however, the bleeding had lasted over several days, and the man's condition was very desperate. However, on opening the abdomen, a very small perforation was found about ten inches from the ileocecal valve.

The intestine was filled with clotted blood, and there was evidence of a great deal of bleeding going on. We opened the intestine and found a distinct bleeding point a short distance from the cecum. The patient's condition was so grave that any further attempt at seeking for the bleeding was thought inexpedient, and we contented ourselves with simply opening the intestine. We

introduced a small drainage tube and packed around this with gauze, which seemed to control the bleeding point without any difficulty. The patient's condition was so desperate that nothing further was done. He succumbed about two hours after the operation, purely as the result of exhaustion following a long and profuse hemorrhage into the bowel.

In referring to the note of the late Dr. Scott, I find he cites this case, so far as he knows, as the first operated on for relief of hemorrhage in typhoid fever. Although in this case, as noted above, we found also a small perforation. We do not hesitate in saying that if this case had been dealt with earlier the unfavorable termination might have been avoided.

Case II. — Wm. J., aged thirty-four years; laborer. Admitted to the Pennsylvania Hospital on February 2, 1908. Diagnosis, typhoid fever. From his admission to the house the patient was very ill and presented all the gravest symptoms of the disease. Three weeks later he complained of pain just below and to the right of the umbilicus. Shortly after, a well-marked hemorrhage from the bowel, amounting to about 13 ounces, manifested itself. Opium was given in large doses. Distention gradually increased, and later liver dulness was obliterated. The pulse was small, about 130. Four hours later he complained of pain and was slightly tender under the middle of the right rectus.

Seen in consultation with Dr. Scott. Abdomen distinctly rigid and presenting all the classical signs of perforation, in addition to the hemorrhage. Operation was advised, although the patient's condition was desperate. On opening the abdomen to the left of the median line, gas and blood escaped. The abdominal cavity was filled with blood. The intestines were deeply injected and covered with flakes of plastic lymph. The intestines were exposed and three perforations made in the ileum. The involved portion of bowel, curiously, was well over to the left side of the peritoneal cavity and held down with numerous adhesions. At the bottom of the pelvis the intestine was very adherent, and the largest of the perforations was found at that point. There was free bleeding from the edges of the perforations, which poured out through the

perforation directly to the abdominal cavity, filling it with blood, so that the condition presented very much the same appearance as in a ruptured ectopic pregnancy.

The segment of bowel in which the bleeding and perforation existed was drawn out to the wound and an artificial anus established, and the wound carefully packed with sterile gauze. An intravenous injection of normal salt solution was given while on the table. The patient reacted very imperfectly, and died at 1 A.M. —twelve hours later.

Something might be said with regard to the question of diagnosis, or more particularly to determining when to operate, and to the consideration of what may be deemed a dangerous hemorrhage.

It may be well to make a distinction between the cases in which only a small amount of blood is passed and those in which there is a considerable quantity, as it is by no means rare for patients to pass small amounts of fresh blood in their stools. These may be in the forms of streaks over the surface of the feces, as from hemorrhoids or fissures, and are usually small in quantity and of bright red color, and are not considered of any serious importance.

Occasionally patients will pass a small single clot, and the amount of blood will not amount to more than a few cubic centimeters. If the stools are carefully examined, these small hemorrhages will be frequently seen, but they cannot be considered as hemorrhages in the true sense.

Where this condition exists the greatest care should be observed in the examination of the dejecta and the patient's general condition, because sometimes these small hemorrhages will precede a large and exhaustive hemorrhage. Again, a distinction should be made between these early hemorrhages, which are rarely serious, and the more serious and frequent ones later. The former are probably due to very small hyperemic patches, and the amount, as before said, is usually very small. They were often regarded by the older observers as rather a favorable symptom.

The time of the more frequent and serious hemorrhages is usually with the end of the second and through the third week,

and the amount lost may vary, as before stated, from a few ounces to a pint or more.

Ordinarily, the diagnosis may be sufficiently plain, as ocular demonstration of the escape of blood from the bowel is only too apparent, but this does not give a correct idea of the amount of bleeding, for sometimes a very large and exhaustive hemorrhage may fill up the colon with very little escape by the rectum to evidence the condition.

As a rule, there is no warning of hemorrhage beforehand. (It was formerly thought that irritating articles of food—apples, etc. —were responsible for causing a hemorrhage, but I question if this is really much of a factor in the case.)

There is little or no difference in the symptoms between hemorrhage occurring during the course of typhoid fever and hemorrhage from any other cause, except that the patient is often very much weaker and in a poor condition to sustain the unusual loss of blood.

The symptoms are practically identical with what we find in hemorrhage from other causes, namely, pallor, coldness of the surfaces of the extremities, presence of sweating, occasional vomiting, the patient often complaining of weakness, the temperature usually falling—the pulse rate rising with it and the quality altering —presenting very much the picture as seen in surgical shock from traumatism with loss of blood.

If a record of the blood pressure has been kept from time to time, a distinct fall in the pressure will be noticed.

What I consider of great importance is the blood picture, as shown by careful microscopic examination. The change in the blood count depends upon the previous condition, and is a valuable index in determining the amount of blood lost.

There is naturally a drop in the hemoglobin and in the number of red cells—from 5,000,000 down to 3,500,000. In an anemic patient, as cited by McCrea, the hemoglobin fell from 56 to 27 per cent., and the red cells from 3,000,000 to 2,000,000 in a day. The leukocytes were unaltered. There is a disposition to slight leukocytosis.

One very important point to be considered in these cases is the coagulation time of the blood in patients who have had hemorrhages. It would appear that the average time in simple cases, *i. e.* (cases which have not had jaundice) is about three and one-half minutes, and it would appear that the average coagulation time was increased about one minute.

The important point, however, to emphasize with the various methods at our command is the determination of when a hemorrhage is of sufficient gravity to warrant surgical intervention, and whether, if the bleeding, if left alone, or treated expectantly, will cease altogether.

Here the skill and experience of the physician in attendance will be taxed to its utmost, and often the advice of a surgeon may be of use, as the latter is more disposed to seek for bleeding points earlier and not trust so much to nature.

It has been recognized (surgically) that exsanguined subjects bear surgical operations badly, and, if cases are to be operated upon successfully, they must be dealt with before the percentage of hemoglobin has fallen so low that any operative procedure would be prohibitory.

The chief difficulty encountered in hemorrhagic cases where no perforation exists will be to locate the bleeding point. The amount of inflammatory thickening, or, better, the most palpable area of ulceration, may be a guide to the seat of the trouble; but this is by no means a safe guide to follow.

If the ileum, beginning at the ileocecal junction, is raised out of the wound, its contents—whether they be fecal or blood clot—gently pressed between the fingers, forcing them forward into the colon or backward into the ileum, and then the emptied intestine held in front of an electric light, it will be seen that the light will be transmitted through all the coats of the intestine, the blood-vessels will stand out distinctly, and, if hemorrhage is actually taking place, the point will be readily located.

In placing the light in front of the intestine, care must be taken to cut off all the rays except those passing through the bowel, so

that the best possible view may be obtained and the operator's eyes not blinded by the superincumbent rays.

For this purpose, a small five-candle power light, usually sold for use around automobiles and motor boats, will be found to be the most satisfactory, as they can be sterilized or wrapped in a sterile towel and used with perfect safety in close proximity to the wound. Any ordinary drop electric light may be used, but they are not easily brought near the wound, and their light is much more difficult to concentrate.

When the bleeding point is found, the hemorrhage can be controlled by the introduction of sutures through the outer coats of the bowel, which, when tied, will constrict the bleeding point and also invert the ulcerated area, so that perforation at this point will be less likely at any future time during the course of the disease.

If, however, it is found impossible to locate any special point from which bleeding takes place, there being an extensive ulceration and a general ooze from a considerable area of mucous membrane, it will be best to open the bowel, establish an artificial anus, and pack off with gauze the inflamed portion of the bowel from the general peritoneal cavity. This procedure will put the bowel at complete rest, and have the same effect on its ulcerated area as a gastro-enterostomy for a bleeding gastric or duodenal ulcer.

In order to ascertain the ease with which the point of hemorrhage could be located, a number of experiments were performed on dogs.

First the ileum of the dog was emptied of its contents and held up in front of an electric light. The light was found to be well transmitted, and all the bloodvessels were readily seen. A small hollow needle connected with the femoral artery of the dog was then introduced into the lumen of the bowel and the blood allowed to flow. The blood, as it entered the intestine, and as it flowed down the ileum, was easily traced.

As the blood in this experiment was greater in amount than would actually be the case in a hemorrhage occurring in an attack of typhoid fever, a second experiment was done by forcing defibrinated blood from a hypodermic syringe through a small needle

and watching it as it passed into the bowel. This was seen with the greatest ease, and also could be traced in its course down the bowel.

A third experiment consisted in passing a fine, hooked needle into the bowel, scratching the mucous membrane and watching the bleeding which resulted from the injury produced. No matter how slight the scratch, the minutest hemorrhage occurring was detected immediately.

At the present time the mortality from perforation when surgically treated ranges from 50 to 60 per cent., and when we realize that this reduction in the mortality has been brought about by surgical means, is it not patent that we must look to surgery to further reduce the mortality of otherwise fatal cases of hemorrhage?

It is a well-known fact that typhoid patients stand operation exceedingly well, and often leave the operating table in far better condition than before the operation was begun. If the perforation cases stand operation so well, does it not seem reasonable to assume that the less seriously complicated cases (those of hemorrhage) would bear the operative procedure even better?

When surgical intervention was first suggested for perforation it was thought by many to be too radical, but now it is accepted as the only proper treatment. I know that these suggestions advocating surgical interference for hemorrhage will also receive adverse criticism, but nevertheless strongly feel that what advance steps are made in the treatment of severe hemorrhage in typhoid fever will be made along the lines suggested in this paper.

In closing, I wish to emphasize that the great difficulty lies in selecting the cases which will require such radical treatment, and believe this only can be accomplished by the careful study of all typhoid fever cases by the surgeon as well as the physician.

DISCUSSION.

Dr. Morris J. Lewis: I have been deeply interested in Dr. Harte's paper, and believe with him that hemorrhage from the bowel and perforation are two of the most serious complications that occur in typhoid fever; but, unlike perforation, where practically every case not operated upon dies, hemorrhage is not followed by such a record of fatality.

I have said for some time that hemorrhage would, when severe, eventually be considered a complication calling for surgical interference, and I believe that the time has arrived when we should seriously consider this procedure.

My experience at the Pennsylvania Hospital has led me to coincide with Dr. Harte in the statement that typhoid fever patients stand abdominal operations well, and therefore look with favor upon operating on cases of serious hemorrhage that do not yield rapidly to medical treatment, and I believe that further study will enable us to decide which cases are suitable for surgical intervention and which not.

Dr. Harte has said that hemorrhage causes 7 per cent. of the deaths in typhoid fever. The statistics of the Pennsylvania Hospital for the last two and one-half years show that out of 1548 cases of typhoid fever, hemorrhage, severe enough to be called a complication, occurred in only 31 cases—a little over 2 per cent., but of these 31 cases, 13 died from the hemorrhage itself—a mortality of 42 per cent., while 5 died of other complications, and 13 recovered. The total number of deaths occurring in this series, from all causes, was 132, or 8.5 per cent., but of the fatal cases, 9.8 were due to hemorrhage. McCrea, in Osler's *Modern Medicine*, states that in 23,271 cases, hemorrhage occurred in 1641, or 7 per cent., and that the fatality of hemorrhage varied according to different authors and in different epidemics from 10 to 30 per cent.

If anyone brings forward the argument that the operation of abdominal section and handling of the bowel is too serious a procedure to be performed for hemorrhage, upon an ill typhoid, I may mention that this was the argument that was used when operation for perforation was first considered. I fear, however, that a thickened, ulcerated bowel may offer more obstructions to the rays of the electric light than Dr. Harte expects, but consider this paper a most valuable one, and one that will serve as an entering wedge for work in this direction.

Dr. Alfred Stengel: What Dr. Harte has said impresses me as being a very valuable demonstration from the point of view of the surgeon in conjunction with the physician. I have sometimes felt that the occurrence of certain types of hemorrhage in typhoid fever was a matter for surgery rather than for medical management. It is undoubtedly true that the mortality in cases of typhoid hemorrhage in general is rather lower than the figures given

for the last two and one-half years. The statement, as I understood it, indicated that 12 per cent. of the cases of hemorrhage died of hemorrhage, which would be very much higher than the figures that others have obtained or that medical experience would generally indicate. Nevertheless, there are cases of a peculiar and especially dangerous type of hemorrhage that any experienced physician will recognize without much difficulty, in which there is exsanguinating bleeding, which repeats itself with rapidity. These are the cases in which I should feel disposed to ask for surgical treatment at once. There are, on the other hand, cases of small hemorrhage in which every physician has recognized that the hemorrhage is often followed by improvement. Unfortunately, however, these are cases in which we can never be certain of the outcome. We are dealing with a type not unlike the type of appendicitis in which, in spite of the mild symptoms in the beginning, serious termination occurs.

But as to the first type with uncontrollable hemorrhage, those who see much of typhoid fever will have a certain degree of certainty. These cases are so generally fatal that surgical operation is extremely desirable. I have asked surgeons to operate in certain cases of that type and could not get them to do it. In view of what Dr. Harte has done, and told us, I feel that surgeons will hereafter feel more disposed to operate. It would be a great misfortune if there should be the tendency to operate freely and indiscriminately in hemorrhage, because the majority of cases, taking all kinds of hemorrhage into consideration, recover, and there is a certain minor proportion of the cases in which the hemorrhage actually does good, cases in which the congestion of the bowels and intestines is diminished. Cases of continuous and uncontrollable hemorrhage are the ones in which Dr. Harte has properly encouraged us to invite surgical aid at once.

Dr. George Erety Shoemaker: It will always be difficult for a man opening an abdomen under such conditions, if the peritoneal coat has not been perforated, to find which ulcer is bleeding, and it is possible that in the development of surgery it will be found that the most feasible method is to switch off the most suspicious ulcerated area of intestine, which is not usually a long one. Rapidity will be essential. The most rapid method is to make an artificial anus, using Paul's tubes, and depend upon restoration of normal function afterward. I do not see the advantage of making an artificial anus if the bleeding point is not located, unless one ultimately resects the ulcer-bearing area and thereby eliminates the bleeding point. No one but a rapid and experienced operator should make the attempt.

Dr. Walter G. Elmer: It is difficult to see a true and correct analogy between perforation of the intestine and hemorrhage of the intestine. If a diagnosis of perforation of the intestine has been made—and it usually can be made with reasonable certainty—a prompt operation is imperative. The

mortality of the accident is about 100 per cent., but every case saved by operation is a direct reduction in the mortality of the disease.

On the other hand, the great majority of the patients suffering from hemorrhage recover—even the cases of excessive hemorrhage have a fair chance of recovery. The surgeon, therefore, must hesitate to operate early in a case of intestinal hemorrhage, nor would he operate for slight or for recurring hemorrhage, provided the patient's condition was still satisfactory, for there is always the hope that at any moment the patient's condition will improve. If the patient's vitality and resistance are rapidly lowered, however, by frequent and excessive hemorrhage, the danger of an operation also increases very greatly. The mortality must be very high, as a result of moving such a patient from his bed to the operating room, making the necessary preparations for an abdominal section, opening the abdomen, and searching for the bleeding point by transmitting light in the manner described. The risk of thus increasing the mortality would, in a large measure, deter us from giving this advice to the members of the patient's family.

The mortality of typhoid fever in the hospitals of Philadelphia, extending over a period of years, is about 10 per cent., and it is exceedingly doubtful if abdominal section for the arrest of intestinal hemorrhage will appreciably lower the mortality of the disease.

Dr. Harte, closing: No doubt my medical friends and the Fellows of the College will think me pretty radical. In hospitals of the first class, it is imperative that, in cases of typhoid fever, the blood pressure be carefully watched and should be marked on the record as regularly as the temperature is marked. Furthermore, I think the laboratories should keep an accurate record of every case that leaves the hospital, not only of the condition of the urine, but of the feces and blood, as to whether any typhoid bacilli exist. Of course, that means much extra labor, and our hospital management will not give the necessary assistance. I believe, however, that in time it will be done. I think the short-circuiting of the intestines spoken of by Dr. Shoemaker is good surgery in certain cases. I see no reason why a distinct point detected coming from a vessel should not be ligated, thus fortifying that portion and preventing the tendency to perforation. I think it is a mistake to wait in cases of hemorrhage in typhoid fever, just as it is a mistake to wait for the perforation. That was the policy pursued in days gone by. The up-to-date physician is loath to wait. I do not advocate all these cases being dealt with surgically. Some seem to benefit by the bleeding, while others bleed continuously, and the earlier these are dealt with the better will be the results. To differentiate between these cases will tax the physician and the surgeon to the utmost.

ANNUAL REPORT OF THE LIBRARY COMMITTEE FOR 1909.

Mr. President: A tragic occurrence has deprived the College of a distinguished Fellow and the Library Committee of its beloved chairman; and it is perhaps fitting, before presenting our detailed report, to express, even though inadequately, our sense of the loss which we as a Committee have sustained. Dr. Harlan was chairman of the Library Committee from 1894 to the time of his death. He infused harmony and confidence into our work. He discharged the duties of his office with zeal and fidelity. He loved the Library and he loved the Library Committee. At our last meeting, the Honorary Librarian, Dr. Frederick P. Henry, offered the following resolution, which was adopted and inscribed upon our minutes:

"*Resolved*, That by the death of Dr. George C. Harlan the Library Committee has lost not only a most efficient member, but also one whose personality endeared him to his colleagues. Elected a member of the Committee on March 4, 1885, he was its senior member, and served as Chairman since February 12, 1894. As a member of the Committee, he was regular in his attendance at the meetings and took an active and painstaking interest in everything connected with the Library; and, as Chairman, he presided with a dignity and urbanity peculiarly his own. It was largely owing to the genial influence of Dr. Harlan that the meetings of the Library Committee, during his long term of service, were not only entirely free from mutual criticism and misunderstanding, but were anticipated as periods of pleasant reunion."

Since the last report of the Library Committee was presented, our truly invaluable collection has been transferred to a place of safety, and the spectre of loss by fire no longer haunts your Committee. The following data in regard to the moving will be of interest:

The moving was begun June 14, 1909, and all the books of the General and Lewis Libraries were packed, carted to the new building, and placed in the stacks by the 6th of July. The card catalogue, curios, current periodicals, S. D. Gross Library, and various pieces of library furniture were moved August 3 to August 5. The delay of four weeks, from July 6 to August 3, was caused by the failure of the contractors to have the rooms ready for occupancy. Only two rooms were ready at the latter date, the Norris Room (Periodical Room) and the room for the S. D. Gross Library.

The books were moved in boxes of a special size, made to order to fit the electric lift in the stacks, two boxes forming a load; capacity of box, about forty volumes; weight, filled, about 140 pounds; carrying capacity of lift 300 pounds.

An "account of stock," *i. e.*, an examination of each book and comparison with the shelf-list, was taken before the books were moved from the old building, and a second account has been taken since the books have been placed in the stacks of the new building, and it was found that one book, a reprint, was lost during the moving:

Allen, Harrison. Studies in the Facial Region. (Reprinted from the *Dental Cosmos.*) Philadelphia, 1875.

The cost of moving the Library was as follows:

Boxes: 201 at 50 cents	$100.50
Trucks and helpers: 38 loads	185.90
Furniture car and helpers: 7 loads	17.50
Extra assistance in Library for packing, unpacking, and arranging books in stacks	520.63
Total	$824.53

In addition to the actual cost of moving the contents of the Library, the following expenditures were made necessary by the moving:

200 extension shelves for stacks, made from shelving in the old building	$70.00
Removing cases from old building, and erecting same in various rooms and basement of new building	287.00
Frames for notices in Library, screens, and doorcheck for office	55.00
Repairs and repainting in stacks	35.97
Total	$447.97

Number of volumes in the Library	81,018
Number of unbound "Reports" and "Transactions"	8,202
Number of unbound "Theses" and "Dissertations"	23,711
Number of unbound pamphlets	70,213

If we count the unbound reports and transactions as volumes, we have 89,220 volumes. The number of unbound theses, dissertations, and unbound pamphlets make together 93,924 separate publications; these may be roughly estimated as equivalent to about 10,000 volumes more, bringing up the total number of volumes in our Library to about 100,000.

Included in the number of volumes reported above are 2627 known as

"reserves," consisting of second copies of some of the more important periodical publications, and 3409 volumes more or less incomplete.

In addition to the above total the duplicates at this date number 1069.

The volumes reported above are divided as follows:

	Bound.	Unbound.	Total.
General Library	60,528	3.362	63,890
Lewis Library	13,492	44	13,636
On permanent deposit:			
S. D. Gross Library	3,372	3	3,375
Library of the Obstetrical Society of Philadelphia	217	0	217
			81,018

Received during the year from all sources, 4641 volumes, 8157 pamphlets, and 25,927 numbers of various periodicals.

Divided as follows:

	Volumes.	Pamphlets.	Journals.
General Library	4276	8142	25,927
Lewis Library	21	0	0
S. D. Gross Library	66	2	0
By purchase, General Fund	114	0	0
In exchange	164	13	0
Total	4641	8157	25,927

Accessions (including 515 volumes "reserve")	3448
Duplicates	1193
Total increase in number of volumes for the year	3448
The "Donors" for the year ending November 1, 1909, number	430

The following is a list of donations of twenty-five volumes or more, and the gifts from the various publishing houses:

	Volumes.
Dr. Barton Cooke Hirst	648
Dr. J. Alison Scott	265
Dr. Edward P. Davis	174
Dr. Hobart A. Hare	84
Dr. William W. Keen	52
Dr. Joseph Price Tunis	50
Dr. S. Weir Mitchell	43
Dr. A. O. J. Kelly	40
Dr. William W. Farr	38

From the Publishing houses of:

P. Blakiston's Son & Co.	22
F. A. Davis Company	11
Lea & Febiger	123
J. B. Lippincott Company	14
R. L. Polk & Co.	1
W. B. Saunders Company	31
William Wood & Co. (New York)	6

The Library is especially indebted to the following gentlemen for 798 volumes of Paris theses:

Dr. James M. Anders.	Dr. D. Brayden Kyle.	Dr. Francis R. Packard.
Dr. A. P. C. Ashhurst.	Dr. R. S. Lavenson.	Dr. William Pepper.
Dr. George Fales Baker.	Dr. Henry Leaman.	Dr. David Riesman.
Dr. Charles W. Burr.	Dr. R. G. Le Conte.	Dr. John B. Roberts.
Dr. John G. Clark.	Dr. Morris J. Lewis.	Dr. G. E. de Schweinitz.
Dr. John B. Deaver.	Dr. Eugene Lindauer.	Dr. J. Alison Scott.
Dr. F. X. Dercum.	Dr. Morris Longstreth.	Dr. Louis Starr.
Dr. Horace Y. Evans.	Dr. D. J. McCarthy.	Dr. L. W. Steinbach.
Dr. Joseph S. Gibb.	Dr. Edward Martin.	Dr. Alfred Stengel.
Dr. John H. Gibbon.	Dr. Arthur V. Meigs.	Dr. Arthur A. Stevens.
Dr. E. H. Goodman.	Dr. Charles K. Mills.	Dr. A. G. Thomson.
Dr. E. E. Graham.	Dr. S. Weir Mitchell.	Dr. James Tyson.
Dr. S. McC. Hamill.	Dr. E. E. Montgomery.	Dr. James C. Wilson.
Dr. Hobart A. Hare.	Dr. John H. Musser.	Dr. W. R. Wilson.
Dr. George C. Harlan.	Dr. T. D. Myers.	Dr. George Woodward.
Dr. Richard H. Harte.	Dr. George W. Norris.	Dr. James K. Young.
Dr. Barton Cooke Hirst.	Dr. William C. Posey.	Dr. Louis Ziegler.

The Library is indebted for large gifts of pamphlets and unbound numbers of periodicals to the following gentlemen:

Dr. Lewis H. Adler.	Dr. C. H. Frazier.	Dr. G. M. Marshall.
Dr. Oscar H. Allis.	Dr. J. S. Gibb.	Dr. Edward Martin.
Dr. A. P. C. Ashhurst.	Dr. J. P. C. Griffith.	Dr. C. K. Mills.
Dr. Henry W. Cattell.	Dr. Hobart A. Hare.	Dr. J. K. Mitchell
Dr. Burton Chance.	Dr. C. J. Hatfield.	Dr. S. Weir Mitchell.
Dr. S. Solis Cohen.	Dr. F. P. Henry.	Dr. E. J. Morris.
Dr. T. V. Crandall.	Dr. W. W. Keen.	Dr. Charles P. Noble.
Dr. John M. Cruice.	Dr. A. O. J. Kelly.	Dr. George W. Norris.
Dr. Edward P. Davis.	Dr. F. P. Krauss.	Dr. Charles A. Oliver.
Dr. C. W. Dulles.	Dr. R. G. Le Conte.	Dr. W. E. Parke.
Dr. David L. Edsall.	Dr. Morris Longstreth.	Dr. William Pepper.
Dr. A. A. Eshner.	Dr. A. W. MacCoy.	Dr. J. H. W. Rhein.

Dr. David Riesman.
Dr. John B. Roberts.
Dr. Joseph Sailer.
Dr. G. E. de Schweinitz.
Dr. J. Alison Scott.
Dr. Wharton Sinkler.
Dr. John M. Swan.
Dr. C. F. Taylor.
Dr. J. J. Taylor.
Dr. W. H. Trueman.
Dr. H. K. Toulmin.
Dr. H. K. Wells.
Dr. J. William White.
Dr. C. S. Witherstine.
Dr. A. C. Wood
Dr. C. B. Worden.
Dr. William Zentmayer.
Dr. M. W. Zimmerman.

And to Messrs. P. Blakiston's Son & Co., Lea & Febiger, J. B. Lippincott Company, William B. Saunders Company, and John Wyeth & Brother.

Of the 679 new publications added to the Library during the past year, forty were written or edited by Fellows of the College.

Twenty-nine volumes were presented by the following authors or editors:

Sir Thomas Lauder Brunton.
Dr. L. Napoleon Boston.
Dr. Burton Chance.
Dr. G. W. Crile.
Dr. Edward P. Davis.
Dr. W. A. Newman Dorland (Editor).
Mr. C. P. Fisher.
Dr. Hobart A. Hare.
Dr. Otto Juettner.
Dr. Henry Leffmann.
Dr. J. Ewing Mears.
Dr. John K. Mitchell.
Dr. A. J. Ochsner.
Dr. William Osler.
R. L. Polk & Co. (Editors).
Dr. W. T. Porter.
Dr. Samuel Pozzi.
Dr. Morton Prince.
Sir James Sawyer.
Dr. Asa M. Stackhouse.
Dr. H. R. Wharton.
Dr. G. Woolsey.
Dr. J. A. Wyeth.

Eighteen volumes were sent by the publishers at the request of the following authors or editors:

Dr. C. W. Bonney (Translator).
Dr. A. P. Brubaker.
Dr. J. C. Da Costa, Jr.
Dr. John B. Deaver.
Dr. Hobart A. Hare (Editor).
Dr. Barton Cooke Hirst.
Dr. Howard A. Kelly.
Dr. H. R. M. Landis (Editor).
Dr. W. T. Longcope.
Dr. Joseph McFarland.
Dr. Francis R. Packard.
Dr. H. W. Stelwagon.
Dr. James Tyson.

Summary of the "Funds:"

	Volumes purchased.	Cost.	Volumes bound.	Cost.
Henrietta Rush Fales Baker Fund	78	$232.49	29	$23.50
Luther S. Bent Fund	25	40.45	11	7.50
William T. Carter Fund	58	179.12	18	12.60
John D. Griscom Fund	88	236.37	24	12.15
William F. Jenks Fund	64	250.07	12	8.40
Oliver A. Judson Fund	11	50.50	..	.....
William V. and John M. Keating Fund	19	25.20	3	1.30
William W. Keen Fund	78	262.43	14	16.30
Library Endowment Fund	166	686.50	..	.....
Weir Mitchell Fund	57	259.54	..	.....
Elizabeth K. Newcomet Fund	27	37.27	9	4.50
William F. Norris Fund	2	11.92	1	1.35
Philadelphia Medical Society Fund	2	22.51	..	.....
Lewis Rodman Fund	30	217.41	7	2.85
John F. Weightman Fund	11	37.33	1	2.20
Caspar Wistar Fund	66	225.88	18	12.75
Total	782	$ 2774.99	147	$105.40
Special Accounts:				
Fund for completing files of journals	78	$254.40	..	$ ..
Journal Association	25	122.05	..	..
New Book Fund	36	74.05	..	....
J. Ewing Mears Account	23	80.91	8	8.80
S. D. Gross Library Account	65	280.84	12	14.00
Total	227	$812.25	20	$22.80

George B. Wood Fund for Library Supplies, stationery, etc. $320.41

Books bound:

1909	1908	Increase
2066 volumes	1025 volumes	1041 volumes

Number of visitors to the Library:

1909	1908	Decrease
10,175	12,166	1991

Fellows of the College 6,419

Number of books consulted in the Library:

1909	1908	Decrease
15,436	22,409	6973

The number of books reported as "consulted in the Library" includes only those supplied on application to the Librarian or his assistants; there

are many more consulted by the Fellows of the College, who have access to the shelves and stacks, of which no record can be kept.

Number of books taken out:

1909	1908	Increase
5171	5064	107

Cataloguing:

Works	Volumes	Cards Written
951	1067	5363

All accessions of books and the more important pamphlets have been catalogued, and each volume accessioned and shelf-listed. 6294 pamphlets have been examined, and 2099 retained and classified.

21,242 volumes have been re-accessioned.

Revision of Catalogue: Number of cards revised, type-written, examined, and alphabeted for the year ending November 1, 1909, 18,482.

We receive at the present time by purchase, in exchange, or as gifts from the editors or publishers, 705 periodical publications, including "Transactions" and "Reports." An increase of 75 for the year 1909 (35 American and 40 foreign).

The following list shows how these are distributed and credited:

	American.	Foreign.
Henrietta Rush Fales Baker Fund	0	30
William T. Carter Fund	1	26
John D. Griscom Fund	4	38
S. D. Gross Library Account	0	4
William F. Jenks Fund	3	33
Journal Association	1	12
Oliver A. Judson Fund	0	6
William V. and John M. Keating Fund	0	1
William W. Keen Fund	3	20
Library Endowment Fund	5	124
J. Ewing Mears Account	0	1
Weir Mitchell Fund	1	43
William F. Norris Fund	0	1
Philadelphia Medical Society Fund	0	4
Lewis Rodman Fund	0	14
John F. Weightman Fund	0	4
Caspar Wistar Fund	3	17
By Purchase	3	17
In exchange	82	76
Editors	84	16
Publishers	28	0
Total	218	487

In addition, we receive current numbers of 175 American, and 70 foreign medical, dental, and pharmaceutical periodicals, in most cases the exchanges of the following journals, which are sent to the Library at stated intervals, through the courtesy of the editors:

American Journal of the Medical Sciences.
Medical Council.
Monthly Cyclopedia and Medical Bulletin.
Therapeutic Gazette.
University of Pennsylvania Medical Bulletin.

We exchange publications with the following schools of medicine (increase of two during past year):

University of Basel.
" Berlin
" Bern.
" Bonn.
" Breslau.
" Erlangen.
" Giessen.
" Göttingen.
" Greifswald.
" Halle.
" Heidelberg.
University of Kiel.
" Königsberg.
" Lausanne.
" Leiden.
" Leipzig.
" Marburg.
" Rostock.
" Strassburg.
" Upsala.
" Würzburg.
" Zurich.

Faculty of Medicine of Bruxelles.
" " Buenos Ayres.
" " Nancy.
" " Paris.
" " Rio de Janeiro.
" " Toulouse.

1030 Dissertations have been added to the Library during the past year.

We have received for the current year ending November 1, 1909, $482.55 in cash from the sale of duplicates, and $112.26 on exchange account with the New York Medical Book Co. There is a balance to our credit with this account of $162.43.

Amount of fines collected from November 1, 1908, to November 1, 1909, $34.50.

The following is a list of the rare medical works, works of special interest, and medals received during the past year:

Incunabula.

Albertus Magnus. Philosophia domini Alberti Magni. Venetiis, Georgium de Arrivabenis, 1496. (Presented by Dr. George Fales Baker.)

Geber. Summa perfectionis magisterii liber trium verborum. (Rome, Herolt, c. 1486.) (Presented by the Estate of Dr. Alfred Stillé.)

Geminiano, Johannes de Sancto. (Gorus.) Summa de exemplis et similitudinibus rerum. Venetiis Gregorium, 1497. (Presented by Dr. S. Weir Mitchell.)

Ludovicus Pruthenus. Trilogium animae non solum religiosis. Nuremberg, Koberger, 1498. (Presented by Mr. Henry C. Lea.)

Mesue Damascenus, Joannes. (Opera omnia.) Venetiis, Novimagii, 1478. (Presented by the Estate of Dr. Alfred Stillé.)

Petrus de Abano. (Conciliator differentiarum philosophorum.) Venetiis, Herbart, 1483. (Presented by Dr. John K. Mitchell.)

Scriptores astronomici veteres. Venetiis, Aldus, 1499. (Presented by Dr. William Osler.)

Silvaticus, Matheus. Liber pandectarum medicinae. Venetiis, Saraceni, 1488. (Presented by Dr. W. W. Keen.)

Works of Special Interest.

Chirac, Paul. Record of Consultations (in Dr. Chirac's own handwriting). Montpellier, 1700 to 1706. (Presented by the Estate of Dr. Alfred Stillé.)

Collection of Letters on Yellow Fever, transcribed by John Redman Coxe, 1794. (Presented by Dr. S. Weir Mitchell.)

Geber. De alchemia dialogo duo. Lugduni, 1548. (Presented by Dr. S. Weir Mitchell.)

Facsimile of the Diploma of Doctor of Medicine granted to Dr. William Harvey by the University of Padua, 1620. (Presented by Dr. J. F. Payne.)

Grove, Robert. Carmen de sanguinis circuitu à Gulielmo Harvaeo anglico primum invento. Londoni, 1685. (Presented by Dr. S. Weir Mitchell.)

Licence and Seal given by the Physico-Medical College of Venice to Dr. Guiseppe Scutellio, 1703. (Presented by Dr. E. B. Hodge, Jr.)

Medals.

Bronze medal struck in honor of Professor Samuel Pozzi, 1905. (Presented by Professor Pozzi, through Dr. W. W. Keen.)

Centennaire de l'Internat en Médecin et en Chirurgie, Hôpitaux Civils de Paris, 1902. (Presented by Dr. W. W. Keen.)

Medal in honor of Dr. Ephraim McDowell and the first ovariotomy, 1809 (Presented by the American Gynecological Society.)

The change in the Library's quarters has necessarily retarded the work in some departments—principally in the revision of the catalogue, re-accessioning the books of the Library, and in the classification of pamphlets. For the same reason there was a decrease in the number of visitors and in the number of books consulted in the Library.

The Committee calls attention to the fact that the Library was moved at a relatively small expense. The successful transfer of the Library and the short time during which the Fellows were deprived of the use of the books—this in the instance of the periodicals extending only from August 3 to August 9—is also a matter of congratulation. The Committee feels that it cannot too highly commend the zeal and ability of our Librarian, Mr. Charles Perry Fisher. The latter not only devoted himself with enthusiasm and singleness of purpose to the task before him, but he also infused this spirit into his assistants. The moving was accomplished safely, expeditiously, and well.

The Committee invites the special attention of the Fellows to the Norris Room (the Periodical Room), the arrangement of which the Committee believes to be quite unique. In this room all the current journals are placed upon open shelves, properly classified, and are most accessible. The attention of the Fellows is also invited to the arrangement of the journals in the Ashhurst Room (the Reading Room). Here are placed upon the shelves the bound volumes of all of the more important periodicals for the last ten years, and it is the intention to carry out this plan as a permanent arrangement. Fellows who are in the habit of looking up the recent literature will realize the enormous convenience of this plan. Finally, the Fellows are already familiar with the special rooms set aside for those engaged in bibliographic research, and it is unnecessary perhaps to comment upon this arrangement further than to say that in the belief of the Committee the service to these rooms will be very satisfactory.

There are now employed in the Library as assistants, one cataloguer, one assistant cataloguer, one assistant to the Librarian, and three boys who are in constant attendance. There are also two temporary employees—one assistant employed in the revision of the catalogue and another employed in the re-accessioning of books.

The Committee has at various times had under advisement the feasibility of opening the Library upon evenings and upon holidays. The question has thus far been one solely of expense.

Based upon the present current expenses of the Library and upon other information the Committee has been able to secure, it is estimated that if the Library were to be kept open in the evening until ten o'clock, Sundays and legal holidays excepted, the privileges being the same as during regular library hours, including the taking out of books, the cost would be about as follows:

Two attendants, one for the Periodical Room and one for the Reading

Room, and two boys, with the supervision of the Librarian, say twice weekly, seventeen hundred and sixteen dollars ($1716) per annum.

If the Library were to be kept open three evenings of each week, say Monday, Wednesday, and Friday, eight hundred and fifty-eight dollars ($858) per annum.

The additional expense of lighting which would be about $30 per month, and the extra services of the hall porter, or assistant to the night watchman, would be a matter for the consideration of the Hall Committee.

If the Library were to be kept open on legal holidays other than Christmas, New Year's Day, Thanksgiving Day, and the Fourth of July, say for half a day, until 1 o'clock P.M., with the necessary service as mentioned above, including the supervision of the Librarian, the expense per annum would be sixty-three dollars ($63); if the Library were open for the entire day, one hundred and five dollars ($105); if for the entire day, including the evening, one hundred and eighty-nine dollars ($189).

The Committee feels that the opportunity of using our great Library should be restricted as little as possible, and it would, therefore, as a move in this direction, recommend to the favorable consideration of the College the opening of the Library for a limited number of evenings and half holidays as soon as the College feels it wise to incur the necessary expense.

The Library has benefited from the Directory for Nurses on an average of $1980 annually during the last ten years. It is greatly to be feared, however, that this source of income will be much impaired by the unavoidable remittance of fees for the furnishing of nurses. Further, the fact must also be recognized that the source of income from the Directory for Nurses must necessarily be uncertain, and cannot be estimated definitely. Finally, your Committee calls special attention to the fact that our endowments, consisting for the most part of small separate funds, are still far from adequate to the maintenance and growing needs of the Library, and that it is greatly to be hoped that the efforts of the Fellows in behalf of the Library will not cease.

Respectfully submitted,

F. X. Dercum,
Chairman.

REPORT OF THE COMMITTEE ON THE MÜTTER MUSEUM, 1909.

The removal of the Museum from the old to the new quarters has been by no means an easy task, because each and every specimen of the collection had to be packed and guarded during the taking down and adapting of the several cases to suit their new positions. This task was satisfactorily accomplished with considerable ingenuity and constant overseeing.

The wet preparations, of which there are several thousands, were thoroughly cleaned, and the old alcohol was substituted by a 5 per cent. solution of formaldehyde, and many jars changed so as to admit of better display of their contents. The numerous valuable osteological and pathological specimens had to be cleaned and packed in boxes and barrels, and they, with the wet preparations, were removed and installed without damage or loss.

The Chairman of the Mütter Committee during the removal took opportunity to personally examine in careful detail the entire collection. He now wishes to impress upon the Fellows of the College the great practical value of the Museum, which should be regarded as an important integral part of the institution, of which, in its new palatial home, we are all justly proud.

Special attention is drawn to the collection of crania and preparations of erosion made by Professor Hyrtl, of Vienna, and obtained directly from him to the unique collection of the comparative anatomy of the ossicles and labyrinth of the ear, to the Politzer collection of diseases of the human ear, and to the preparations by M. Trammon, showing the progressive stages of dentition. Particularly interesting are the collection of casts of the Peruvian skulls, showing the very early practice of trephining, presented by Dr. S. Weir Mitchell; and, most valuable of all, because the rarest, is the collection of Sappey's injections with mercury of the lymphatic vessels. There are many other interesting features, which render the Museum serviceable for reference and study.

The Committee has found pleasure in the thought that in the care it has given to the rearrangement of this valuable material it has helped to perpetuate the memory of Dr. Thomas D. Mütter whose own private accumulation of specimens, given to the College, together with an income intended

to maintain and increase the Museum, entitles his name justly to stand at the head of the list of eminent benefactors of this institution.

A special case has been set aside in memory of Professor John H. Brinton, who was for many years Chairman of the Mütter Committee, and was earnestly devoted to the welfare of the Museum. It contains the private collection of Professor Brinton, used by him in his teaching, and contains a number of rare specimens of fractures.

The Chairman feels that the time and trouble which have been expended was in great measure compensated by the kind words of Dr. Collins Warren, of Boston, who, when he was here at the time of the festivities attending the opening of the new building, voluntarily exclaimed: "It is a thoroughly up-to-date museum for practical use, and has much that is unique and without equal."

The Chairman ventures to call attention here to some facts which are little known.

It is recorded in the minutes of the Mütter Museum Committee that for twenty-two years (1863–1885) Dr. Mitchell was a constantly present member at its meetings, and that to his foresight and clear judgment are due the acquisition of nearly every one of the valuable collections which have been enumerated. In behalf of the Museum, therefore, its present Committee would like to render to Dr. Mitchell the thanks that are surely due him, and although they may seem humble in comparison with the many testimonials he has of greater worth, they are equally sincere. The Committee also ventures to remind Dr. Mitchell and the College that the Museum specimens are nature's books, and that the Museum itself is a library of records, containing not merely copies, but dissimilar and varied originals by one acknowledged author.

The Mütter Committee will have the Museum open for inspection and consultation at certain hours every day of the week, when the Curator will be in attendance, and at other times when desired, by appointment.

The Mütter Committee wishes to express their sorrow at the loss of their colleague, Dr. J. Alison Scott, whose illness deprived it of the assistance of his suggestion and advice, and whose death was an irreparable loss. Dr. Scott's kindly nature, added to his good judgment, made his personality warmly appreciated by all who had the good fortune to come in contact with him.

During the bustle of moving no attempt was made to add to the collection. A number of vesical calculi and surgical instruments formerly belonging to Dr. John B. Methuen, of Richmond, Va., have been presented by Dr. Geo. Ben Johnson.

At all times contributions of specimens will be welcome, and, if passed upon favorably by the Committee, will be added to the cabinets.

The regular Mütter Lecture was given by Dr. Henry D. Fry, Professor of

Obstetrics Georgetown University, Washington, D. C., December 10. The subject of his address was: "The Nutritional Changes Occurring in Fibromyomata of the Uterus Incident to Pregnancy and the Puerperium." It was delivered in the Cadwalader Room, adjoining the Museum, to a large and attentive audience.

Respectfully submitted,

GEORGE MCCLELLAN,
Chairman.

LIST OF PAPERS: SECTION ON OPHTHALMOLOGY.

December, 1908.

Report of a Case of Opticociliary Vein, by Dr. William T. Shoemaker.

Concerning the Disappearance of the Coloration in Sidereosis Bulbi, by Dr. G. E. de Schweinitz.

Epithelioma of the Eyelid of Somewhat Unusual Form and Development, Together with the Results of Operative and *X*-ray Treatment (Exhibition of the Patient), by Dr. G. E. de Schweinitz.

Recurrent Pterygium Treated by Removal and the Implantation of a Thiersch Graft (Exhibition of Patient), by Dr. G. E. de Schweinitz.

Herpes Zoster Ophthalmicus, with Involvement of the Cornea and with Oculomotor Paresis, by Dr. Burton Chance.

Exhibition of a Case Showing Angioid Streaks in the Retina, by Dr. William Zentmayer.

The Visual Acuity Under Definite Condition is an Index of the Strength of the Necessary Spheric Lens (+ or —) Which Will Give a Vision of 6/6 or More, by Dr. James Thorington.

Exhibition of a Patient Showing a Foreign Body of Unusual Size Within the Eye, by Dr. William M. Sweet.

January, 1909.

Exhibition of a Case of Intra-ocular Neoplasm, Probably a Solitary Tubercle of the Choroid, by Dr. Wm. Campbell Posey.

Exhibition of a Case of Palsy of the Levator from Frontal Sinusitis, by Dr. Wm. Campbell Posey.

Exhibition of a Case of Glaucomatous Excavation Due to Syphilis of the Optic Nerves, by Dr. Wm. Campbell Posey.

Exhibition of a Patient Showing Postneuritic Optic Atrophy in Syringomyelia, by Dr. Edward A. Shumway.

Choroidal Hemorrhage Following Operations on the Globe, by Dr. Wm. Campbell Posey.

Exhibition of a Case of Unilateral Exophthalmos, by Dr. G. E. de Schweinitz,

Two Cases of Hole at the Macula, by Dr. William Zentmayer.

Exhibition of a Patient Showing Choroiditis from Antral Infection, by Dr. S. Lewis Ziegler.

February, 1909.

Exhibition of Patients after a Kuhnt-Szymanowski Operation Had Been Practised for the Relief of Senile Ectropion, by Dr. G. E. de Schweinitz.

Demonstration of a Patient Showing a Perfect Result after a Bilateral Simple Extraction of Cataract, by Dr. G. E. de Schweinitz.

Exhibition of a Case of Double Cupping of the Nerve-head in a Case of Chronic Non-congestive Glaucoma, by Dr. George S. Crampton.

Persistent Pains after Enucleation, Apparently Hysterical, by Dr. S. D. Risley.

Nodular Opacities of the Cornea, with Exhibition of the Patient, by Dr. William Zentmayer.

Wound of the Left Orbit, Followed by a Partial Oculomotor Palsy and Paralysis of the Trochlearis; Recovery, by Dr. G. E. de Schweinitz.

Suppurative Ethmoiditis, by Dr. Frederick Krauss.

Avulsio Bulbi, by Dr. Carl Williams.

Demonstration of a New Eye Speculum, by Dr. William T. Shoemaker.

March, 1909.

Report of a Case of Uremic Amaurosis Following Scarlet Fever, by Dr. A. C. Sautter.

Report of a Case of Steel Injury of the Eye, by Dr. T. B. Holloway.

A Case of Unilateral Retrobulbar Neuritis Due to Ethmoiditis, with Restoration of Vision, by Dr. Frederick Krauss.

The Ocular Symptoms of Barlow's Disease, with the Report of a Case, by Dr. J. Hiland Dewey.

Report of a Case of Keratitis, Probably Due to Metastatic Gonorrhea, by Dr. Wm. Campbell Posey.

April, 1909.

A Case of Retinitis Punctata Albescens in a Negro, by Dr. W. C. Swindells.

Exhibition of a Boy after the Removal of the Lacrymal Sac on Account of Chronic Dacryocystitis, by Dr. Wm. Cambpell Posey.

Exhibition of a Patient after Krönlein's Operation for Orbital Growth, by Dr. Wm. Campbell Posey.

Report of a Case of Unusual Atrophy of the Iris, by Dr. H. G. Goldberg.

Exhibition of a Patient with Ocular Symptoms Simulating Those of Exophthalmic Goitre, by Dr. T. H. Weisenberg and Dr. William Zentmayer.

The Report of a Case of Parenchymatous Keratitis in Acquired Syphilis, by Dr. Burton Chance.

Exhibition of a Calcareous Lens from a Shrunken Globe, by Dr. Burton Chance.

October, 1909.

Proptosis of the Eye, Probably Due to Tuberculous Involvement of the Orbit (Exhibition of the Patient); by Dr. S. D. Risley.

Detached Retina Replaced by Scleral Puncture; Recurrence, by Dr. J. N. Risley.

A Case of Temporary Monocular Amblyopia, Possibly Due to Embolus in the Optic Nerve, by Dr. H. F. Hansell.

Parinaud's Conjunctivitis, with Unusual Complications, by Dr. Frederick Krauss.

Exhibition of a Patient with V-shaped Iridotomy, by Dr. William Zentmayer.

November, 1909.

Clinical Report of a Case of Chronic Sympathetic Ophthalmitis, with Recovery (Exhibition of Patient), by Dr. George Friebis.

Exhibition of a Patient Showing Intense Neuroretinitis Probably Due to Chlorosis, by Dr. Wm. Campbell Posey.

Exhibition of a Case of Mucocele of the Frontal and Ethmoidal Cells, Operated upon by Orbital Incision, by Dr. Wm. Campbell Posey.

Exhibition of a Patient with Hydrocephalus and Ectopia Pupillæ, by Dr. S. D. Risley and Dr. T. H. Weisenberg.

Cyclodialysis, by Dr. Walter L. Pyle.

A Clinical Note on the Relationship of Certain Forms of Skin Disease and Choroiditis, by Dr. G. E. de Schweinitz.

Bilateral Optic Atrophy, Associated with Enlarged Accessory Sinuses, by Dr. H. M. Langdon.

Monocular Hemianopsia Due to Ethmosphenoidal Disease, by Dr. Frederick Krauss.

T. B. Holloway,
Clerk.

LIST OF PAPERS: SECTION ON OTOLOGY AND LARYNGOLOGY.

December, 1908.

Dr. Walter Roberts read a Report of a Case of Temporosphenoidal Abscess. Operation. Recovery. Presentation of Patient.

Dr. S. MacCuen Smith read a Note on Mastoid Pain.

Dr. Joseph S. Gibb read a paper on The Treatment of Recurring Attacks of Lacunar Tonsillitis. Description of the Removal of Submerged Tonsils by Dissection and Snare.

January, 1909.

Dr. G. Hudson-Makuen read a paper on Paresis of the Soft Palate and Other Articulatory Organs, with illustrative cases.

Dr. B. Alexander Randall read a paper on A Word for More Conservatism in Mastoid Inflammation.

Dr. Ralph Butler read a paper on Slides Further Illustrating the Histology and Topography of the Tympanum.

February, 1909.

Dr. Barton H. Potts presented a Patient Showing Result of a Plastic Operation Following a Mastoid Operation.

Dr. Barton H. Potts reported a Case of Purulent Labyrinthitis. Operation.

Dr. Charles P. Grayson read a paper on Some Skiagraphic Fallacies in Sinus Diseases.

March, 1909.

Dr. Barton H. Potts presented a Case of Osteomyelitis of the Frontal Bone.

Dr. Francis R. Packard presented Patients Showing Results of the Killian Operation.

Dr. Alexander W. MacCoy read a Note on the Conservative Treatment of Suppuration of the Accessory Sinuses of the Nose.

Dr. George C. Stout read a paper on Some Experiences with the Bronchoscope.

Dr. George Fetterolf reported a Case of Accessory Thyroid at the Base of the Tongue.

April, 1909.

Dr. George B. Wood presented a Patient Showing Results of *X*-ray Treatment of Papilloma of the Larynx.

Dr. A. A. Bliss read a paper on Nerve Reflexes Simulating Local Inflammation.

Dr. George B. Wood read a paper on A Few Suggestions Concerning the Diagnosis of Accessory Sinus Disease.

Dr. James A. Babbitt read a paper on Paths of Infection to the Antrum of Highmore, with Report of a Case.

Dr. S. MacCuen Smith and (by invitation) Dr. A. Spencer Kaufman read a Report of a Complicated Case of Acute Mastoiditis of Unusually Rapid Progress, Resulting Fatally. Autopsy.

May, 1909.

Dr. George B. Wood read a Report of a Case of Carcinoma of the Tongue. Exhibition of the specimen.

Dr. D. Braden Kyle read a Report of Five Cases of Retropharyngeal Abscess.

Dr. B. Alexander Randall read Notes on the Clinical Pathology of the Drumhead.

Dr. Joseph S. Gibb read a paper on Intratympanic Hemorrhage in Typhoid Fever, with report of a case and presentation of specimens.

Dr. James Babbitt presented a Case of Modified Killian Operation on the Frontal Sinus.

October, 1909.

Dr. George B. Wood read a Report of a Case of Sarcoma of the Tonsil, with presentation of patient.

Dr. Francis Packard read a Report of a Fatality Following Removal of Tonsils and Adenoids.

Dr. Walter Roberts read a Report of a Case of Extensive Thrombosis of the Lateral Sinus Affecting the Cavernous Sinus, with presentation of patient.

Dr. Charles P. Grayson read a paper on Some Revised Diagnoses.

Dr. George Morley Marshall read a paper on Urano-Staphyloplasty Three Weeks After Operation. Exhibition of case. Discussion was opened by Dr. G. Hudson-Makuen.

Dr. B. C. Gile (by invitation) read a Report of a Case of Gumma of the Nose, with presentation of patient.

November, 1909.

Dr. George Coates read a paper on Results of the Radical Operation for Suppuration of the Frontal Sinus, with exhibition of a case.

Dr. B. Alexander Randall read a paper on Another Gibe at Heredity.

Dr. James A. Babbitt read a paper on Adenectomy and Tonsillectomy upon Infants.

Dr. Joseph Tunis exhibited some Stereoscopic Views of the Ear.

RALPH BUTLER,
Clerk.

LIST OF PAPERS: SECTION ON GENERAL MEDICINE.

January, 1909.

Exhibition of Some Specimens of Pulmonary Fibrosis, by Dr. H. R. M. Landis.

The Treatment of Acute Infectious Diseases with Extracts of Leukocytes (Hiss), by Dr. Samuel W. Lambert, of New York (by invitation).

Exhibition of a Patient with an Aneurysm of the Aortic Arch, Treated by Wiring, by Drs. T. Mellor Tyson and R. S. Lavenson.

March, 1909.

A Case for Diagnosis: Thoracic Aneurysm or Dilated Auricle, by Dr. S. Solis Cohen, Discussion of Radiograms, by Dr. Manges (by invitation), and of the Pulse Tracings, by Dr. Bachmann (by invitation).

A Case of Cirrhosis of the Liver, with Subdiaphragmatic Hydrothorax, by Dr. Alfred Hand, Jr.

A Case of Cardiospasm, with Dilatation of the Esophagus, by Drs. M. H. Fussel and R. L. Pittfield.

A Case of Gastric Carcinoma Involving the Pancreas, with a Positive Cammidge Reaction, by Dr. Herman B. Allyn.

A Case of Oligopnea in Advanced Pulmonary Tuberculosis, by Dr. Charles M. Montgomery (by invitation).

Two Cases of Myxedema, by Dr. R. L. Pitfield.

April, 1909.

A Case of Sigmoid Diverticulitis, with Some Observations upon the Diagnosis, by Dr. Sherborne W. Dougherty.

Acute Gout (Podagra) Occurring in a Patient with Bright's Disease while upon a Greatly Restricted Diet, by Dr. David Riesman.

Observations on Gastric Secretion in a Child with a Gastric Fistula, with Remarks upon the Recent Advances in the Physiology of Gastric Secretion and Motility, by Dr. R. S. Lavenson.

Critical Analysis of Typhoid Fever Cases at the Presbyterian Hospital, by Drs. J. C. Gittings and Ralph Pemberton.

GEORGE W. NORRIS,
Clerk.

LIST OF PAPERS: SECTION ON MEDICAL HISTORY.

November 30, 1908.

Dr. W. W. Keen, Remarks on the Incunabula and Other Books Purchased for the College during My Stay in Europe, and also on the Sepulchral Mural Tablets of Bologna; Exhibition of Incunabula and Photographs of the Mural Tablets.

Dr. Chas. W. Burr, Some Remarks on the Life of Jerome Cardan.

Dr. James J. Walsh, Professor of the History of Medicine at Fordham University School of Medicine, Old-time Medicine and Medical Education.

WILLIAM PEPPER,
Clerk.

NEW HALL OF THE COLLEGE OF PHYSICIANS OF PHILADELPHIA

Twenty-second Street above Chestnut

DESCRIPTION OF THE MEDAL TO COMMEMORATE THE OPENING OF THE NEW BUILDING OF THE COLLEGE OF PHYSICIANS

By R. TAIT McKENZIE, M.D.

Obverse. A youth typifying the future stands over the motto of the College: "Non sibi sed toti" (not for himself but for all). His eyes are directed downward toward a chart which he has spread out to display an embossed representation of the front elevation of the new building. On the ground the dates 1787 and 1909 give the founding of the College and the opening of the new building. The circular inscription in the margin reads: "College of Physicians of Philadelphia."

Reverse. A tripod ornamented with rams' heads, bearing a lighted lamp with divergent rays. Curiously entwined in the legs a serpent raises its head to the light, typifying the profession rising to the light of learning. The inscription in parallel bands is:

> "For advance in medical learning,
> integrity in the profession, and
> the relief of human suffering."

It is signed by a monogram, "R. I. M."

1787 1909

EXERCISES ON THE OCCASION

OF THE

DEDICATION OF THE NEW HALL

OF THE

COLLEGE OF PHYSICIANS OF PHILADELPHIA

NOVEMBER TENTH AND ELEVENTH

MDCCCCIX

EXTRACT FROM THE ORIGINAL CHARTER.

"And whereas, the objects of this College are to advance the science of medicine, and thereby to lessen human misery, by investigating the diseases and remedies which are peculiar to this country; by observing the effect of different seasons, climates, and situations upon the human body, by recording the changes which are produced in disease by the progress of agriculture, arts, population, and manners; by searching for medicines in the American woods, waters, and in the bowels of the earth; by enlarging the avenues to knowledge from the discoveries and publications of foreign countries; and by cultivating order and uniformity in the practice of physics."

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1909.

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HENRY MORRIS, M.D.

* Died September 25, 1909.
† Died August 13, 1909.

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Marshals.

Dr. Astley P. C. Ashhurst
Dr. J. A. Bayard Kane
Dr. Henry R. M. Landis
Dr. Joseph McFarland

ORDER OF EXERCISES.

Wednesday, November 10, 2 P.M.

Assemblage of Fellows and Guests at the First Unitarian Church.

Procession to the Entrance of the New Hall.

PRESENTATION OF THE NEW HALL.

By Dr. William J. Taylor, Secretary of the Building Committee.

ACCEPTANCE OF THE NEW HALL.

By Dr. George E. de Schweinitz, Vice-President.

ADDRESSES.

Robert Fletcher, M.D., Library of the Surgeon-General's Office.

John Shaw Billings, M.D., New York Public Library.

Charles Loomis Dana, M.D., Academy of Medicine of New York.

Reginald Heber Fitz, M.D., Boston Medical Library.

William Sydney Thayer, M.D., Medico-Chirurgical Faculty of Maryland.

Frederick P. Henry, M.D., Honorary Librarian, Library of the College of Physicians of Philadelphia.

CONFERRING OF ASSOCIATE FELLOWSHIPS.

Archibald Byron Macallum, M.A., M.B., Ph.D., Sc.D., LL.D., F.R.S.
To be presented by Albert Philson Brubaker, M.D.

Oliver Fairfield Wadsworth, M.D.
To be presented by George Edmund de Schweinitz, M.D.

Edward Gamaliel Janeway, M.D., LL.D.
To be presented by James Cornelius Wilson, M.D.

Charles Loomis Dana, M.D.
To be presented by Charles Karsner Mills, M.D.

Frank Billings, M.D.
To be presented by John Herr Musser, M.D.

George Washington Crile, M.D.
To be presented by William Louis Rodman, M.D.

Franklin Paine Mall, M.D.
To be presented by George Arthur Piersol, M.D.

DEDICATORY ADDRESS.

By the President, Dr. James Tyson.

BENEDICTION.

By the Rt. Rev. Ozi W. Whitaker, Bishop of Pennsylvania.

Thursday, November 11, 1909,

10 A.M. to 2 P.M.,

Inspection of the New Hall.

8 P.M.

Address by S. Weir Mitchell, M.D., LL.D.

Followed by a Reception.

PRESENTATION OF THE NEW HALL

By WILLIAM J. TAYLOR, M.D.,
SECRETARY OF THE BUILDING COMMITTEE.

Eight years ago our library had outgrown the space allotted to it in our old home at Thirteenth and Locust Streets, and the building in other respects was no longer sufficient for our needs.

Largely through the efforts of one of our Fellows generous subscriptions were obtained from many of our Fellows and from friends of the College in this and other cities, with which the lot was purchased in 1903.

A period of years then passed before sufficient funds could be secured with which to build and equip a fitting home for this the oldest of American medical societies. Many generous friends, however, came to our aid, and in January, 1908, the ground was broken, and the cornerstone laid in the following April.

The construction and furnishing was intrusted by vote of the College to a committee, who, with the architects and contractors, have labored faithfully and cheerfully these many months.

It is now, Mr. Vice-President, my very pleasant duty and great privilege to deliver to you, on behalf of the Building Committee, the keys of this large and beautiful building, complete in every detail and ready for the use of the College.

ACCEPTANCE OF THE NEW HALL.

By G. E. de SCHWEINITZ, M.D.,
VICE-PRESIDENT.

Since the second day of January, 1787, when nine senior and four junior Fellows of the College first met after its full organization, until the present time, five homes have sheltered the members of our guild and housed the treasures of our library—treasures that once could be stored in a single case, and now are counted by well nigh 100,000 volumes.

Today, Mr. Secretary, in accordance with the instructions of the committee in charge of these exercises, and on behalf of the President and officers, and in the name of the Fellows of the College of Physicians, I have the honor, the very great honor, to accept this new home, "of mark beyond all others"—to accept it with pride in the nobility of its structure, with satisfaction in the amplitude of its unrivalled equipment, with rejoicing in the completion of its brave and generous plans, but not forgetting in this full hour rich in the joy of present achievement our heritage of greatness and the example of our predecessors.

As spokesman of the Fellows of the College, I desire to express our high appreciation of the work of the architects and of the builders, consummated in this notable example of their professional and technical skill; to convey our deep sense of obligation to the Funds Committee for the task it has so well performed; to congratulate the Hall Committee and the Librarian on their successful transference of our possessions from the old College to the new; and to thank with heartfelt gratitude all those who of their generosity have contributed in the erection of this great edifice.

But, Mr. Secretary, my words of acceptance of this new building of the College of Physicians would be far from complete did I not in public acknowledgment emphasize the relation of the Building Committee to this splendid fulfilment of our desires. The members of this committee, and you in particular, their chief executive officer, have striven so earnestly, so effectively, so unselfishly, that they have placed all those who hereafter shall share in the benefits of these new surroundings deeply in their debt.

In token of what has been so well accomplished, I pray you accept my hand and these all too feeble expressions of our lasting obligation and loving regard.

ADDRESS OF ROBERT FLETCHER, M.D.,[1]

LIBRARY OF THE SURGEON-GENERAL'S OFFICE.

A RARE REPRINT OF A RARE WORK OF VESALIUS.

The time that may be occupied on this interesting occasion will not allow of any but a mere allusion to the treasures of the Library of the Surgeon-General's Office at Washington. By comparison of the number of books and pamphlets in its possession it ranks, I believe, as second in the exclusively medical libraries of the world. It has been forcibly said that you cannot judge of the quality of the timber by counting the trees in the forest, so the standard of comparison by counting the number of volumes in a library is but approximate.

I propose to describe briefly a choice recent addition to our collection of the works of Vesalius. The epoch which marks the production of the great work of that author, *De Corporis Humani Fabrica*, in 1543, has been admirably stated by Sir Michael Foster, who says:

"The 'new birth' of the fifteenth and sixteenth centuries was, in essence, a revolt against authority as the guide in knowledge, and the work of Andreas Vesalius . . . marks an epoch, since by it the idol of authority in anatomical science was shattered to pieces, never to be put together again. Vesalius described the structure of the human body such as he found it to be by actual examination, by appealing to dissection, by looking at things as they are. He dared not only to show how often Galen was wrong, but to insist that when Galen was right he was to be followed not because he had said it, but because what he said was in accordance

[1] In the absence of Dr. Fletcher his paper was read by the Secretary of the College, Dr. Thomas R. Neilson.

with what anyone who took the pains to inquire could assure himself to be the real state of things."

To this may be added an amusing instance of the extravagant adulation of the Galenists for their master. Silvius, when forced to admit the inaccuracy of one of Galen's descriptions, replied that "Man had changed, and not for the better."

Time will not permit me to dwell upon the career of Vesalius, nor to speak of the various editions and translations of his great work, but I may draw your attention to one of his publications, so rare that only two copies are known to be in existence. This is the *Tabulæ Anatomicæ Sex*, printed at Venice in 1538, and which was intended by its author to be a forerunner of his great work, which latter did not appear until 1543. An exquisite fac-simile reprint of the *Tabulæ* was made through the generous zeal of Sir William Stirling-Maxwell, a Scottish gentleman of large estates and long descent. The book is elephant folio in size, its exact dimensions being 20 x 27 inches. Its date is London, 1874. Only thirty-two copies were printed—one on parchment, one on vellum, and thirty on paper. They were kept for private presentation only, and I believe no copy has ever found its way into the book market. The present baronet, Sir John Stirling-Maxwell, the son of Sir William, had but six copies in his possession recently when he presented one of them to this library through the instrumentality of Dr. Osler. Sir William Stirling-Maxwell was born in 1818, and died in 1878. He is best known in literature by three of his works, namely, *Annals of the Artists of Spain*, *The Cloister Life of the Emperor Charles V*, and *Don John of Austria*. A collected edition of his works was issued, in six volumes, in 1891.

The Vesalius reprint is composed as follows:

1. A presentation page, with a colored border, by Weigel, intended to contain the autograph of Sir William.

2. The title page, which is a fac-simile of the fine title page of the copy on vellum in the British Museum of the *De Humani Corporis Epitome*. This is the same title page as that of the great work itself of 1543. It represents Vesalius lecturing on the dead

body of a woman before a strange assembly of men, both old and young. One student is suspiciously like a woman, and a naked boy is taking a surreptitious view from behind a pillar.

3. The fine wood-cut portrait of Vesalius, by Johan-Stephan von Calcar, who executed the drawings for the great work, which were for a long time attributed to Titian. Calcar was a fellow countryman of Vesalius, both having been born in the Duchy of Cleves.

4. A sketch of the life of Vesalius, by Sir William Stirling-Maxwell.

5. The six anatomical plates.

I infer from Dr. Osler's letters to me that this interesting reprint, which I have ventured to describe to you, is the only copy in the United States. An additional point of interest is suggested, that the plate showing the liver as the origin of the veins, being the Galenical view, is the only such illustration known.

ADDRESS OF JOHN SHAW BILLINGS, M.D.,

NEW YORK PUBLIC LIBRARY.

I TAKE great pleasure in presenting to you the congratulations of the New York Public Library upon this happy occasion. You have at last, after much delay, obtained this very handsome and conveniently arranged building, in which the treasures which you have accumulated can be properly cared for and made available for your use. And I speak of these treasures with some knowledge of what they really are, since for the last forty years I have been well acquainted with the library of the College of Physicians. In fact, my earliest training in medical bibliography was obtained in the study of its catalogues and of your collections, and I know that you have a very complete summary of medical science as it exists today. Not quite so large, it is true, as some other collections, but still ample for almost every purpose of medical research.

And I offer the congratulations, not only of the New York Public Library, but those of all other large public libraries, on your success in obtaining and properly housing this most valuable collection.

And to this I may well add congratulations to the Public Library of Philadelphia that it has such a medical library at hand; for, in those cities which have a public library but no medical library, it becomes the duty of the public library to provide something of medical literature for its patrons, and this is a most difficult matter. It is a great comfort to be able to send laymen and laywomen who want information on such matters as generation, sex, and heredity to a library which is under the direction of experts and in which you are reasonably sure they can be furnished with all the information which they ought to have, if not, perhaps, all the informa-

tion which they think they desire. And this library is perhaps the most complete one in the world on these subjects, as it has the special collection made by the late Dr. John Stockton Hough.

May the good work and merited fame which has characterized the College for so many years continue and increase in this its new home.

ADDRESS OF CHARLES LOOMIS DANA, M.D.,

ACADEMY OF MEDICINE OF NEW YORK.

The New York Academy of Medicine sends to the College of Physicians of Philadelphia fraternal greetings. I am called here, in the fashion of Hermes, as a messenger of the high gods at home, and I bring their tribute of good wishes and congratulations upon your present great achievement.

In bringing such message, I speak with a note of real personal feeling, and not alone as the representative of a kindred institution; for I know the work and worth of this College, with its storied past, and have had experience of its helpfulness and hospitality.

I thank you for the high honor you are conferring upon me, but shall take it as in large part a tribute to the Academy from which I come.

It is, I understand, my function at this time not to praise my hosts, but to do the less grateful task of telling them something of the organization from which I bring these gifts of cordial words.

The New York Academy of Medicine was organized in 1847, and is thus by sixty years the junior of this College. It did not inherit history, and has had, therefore, to make it. It owes its existence, in a way, to the widows and orphans of medical men, and its origin shows how the poor and the humble may be an inspiration to mighty things. It was at a meeting of the members of the society for helping these widows and orphans that the idea of organizing the New York Academy of Medicine originated. The purpose was to establish a society which should stand for high aims in medicine, which should encourage efforts to keep our art free from charlatanry, and unite those who had truly at heart the best interests of the profession.

The Academy worked modestly for many years, and carried out

measurably well its ideals. It was through its efforts that New York City first organized a Board of Health; and the Academy has, since its beginning, initiated or aided nearly every measure for the advancement of public health and the promotion of medical science. The great physicians and surgeons whose work has made medical history in New York have had the Academy for their forum.

A new and most impelling force was given to our organization when it began, in 1876, seriously to collect a medical library. From that time its growth became much more rapid and its work especially efficient.

A second impetus of almost equal importance came when, eighteen years ago, in lusty adolescence, we also acquired a new Hall. The recollection of what our Academy building did for us compels me to emphasize again the congratulations on your present achievement. Under the inspiration of high ideals, with the helpful stimulus of a great library, and an adequate and attractive home, the New York Academy has grown in its six decades from a membership of 184 to one of over 1000, and it has a waiting list besides. Its library has increased in thirty-three years from 400 volumes to over 80,000, and to it are made every year over 16,000 visits. Its scientific work is done in bi-weekly general meetings and in monthly meetings of its thirteen special sections. It has an adequate income and owns its halls. It is a great force for good in the city of New York. This is surely enough to say of my own Academy, whose prosperity and usefulness I will admit to be only inferior to your own.

Let me carry you back a moment now into the history and allegory of the past. In the middle of the sixteenth century there lived a certain Dr. John Phillip Ingrassus, who was known as the Hippocrates of Sicily. He translated and published the *Ars Medica* of Galen. In praise of this wonderful book, Franciscus Guastella, who admits that he was "one of the least of the disciples of God," wrote a song. It was addressed, three hundred and fifty years ago, to the readers of this single book, Galen's *Art of Medicine.* He says, *ad lectorem:*

"If you wish to see the whole Art of Medicine,
Run to this Light; and fly quickly,
For whoever you are that reads here, you will desire to be a logician,
A philosopher, a physician, and finally, a wise man."

FRANCISCUS GUASTELLA.
Ad Lectorem Carmen.

"Sique videre cupis totam medicinæ scilicet artem,
Hoc curre ad lumen, moxque fuge.
O, quicunque legas, logicus, cupes esse, Phillipum.
Atque Sophus, medicus, denique sapiens."

The times have changed, for this one book, which told the art of medicine, this *Ars Medica* of Galen, is now represented by 90,000 volumes, such as are in the Library of the College of Physicians of Philadelphia; but the urgent moral is the same. If you wish now to see the whole Art of Medicine, "fly to this light" of the College of Physicians, and "fly quickly" (*moxque fuge*). And we are here.

The College of Physicians, like the Academy of New York, has a medical library of extraordinary value and completeness. This here, as with us, is the special treasure which brings the workers to these doors. Yet the ceremonies of this hour show that the fame of the work done by this College, and the eminence of the great names which adorn its history, are a treasure of still more moment and imperishable value.

In 1710 Prof. Lancisi, of Rome (he of the *Striæ* that wind along the Corpus Callosum), presented, with formal ceremonies, a great medical library of 20,000 volumes to the Hospital San Espirito. It was the first specific opening and dedication of a medical library, so far as I can learn, in the history of the world. His friend, Ramuzzini, Professor of Medicine at Padua, and author of an immortal work on the *Diseases of Learned Men*, wrote what he called "a pleasant epigram" for the occasion. He says:

"You complete the great work you have undertaken, my Lancisi, and you dedicate it, as is the custom of the City, to a sacred use.
Here anyone may be able to peruse the monuments of the wise, however many Italy or Greece possesses.
Here these works shall be kept, great friend, but this library will not be able to contain and circumscribe thy fame."

RAMUZZINI TO LANCISI ON THE DEDICATION OF HIS LIBRARY.

"Grande opus agressus, Lancisi, perficis atque
Addicis sacro, mos ut in urbe, loco,
Perlegere hic quisquis poterit monimenta Sophorum,
Quotquot habet Latium, Græcia quotquot habet.
Hic tua perstabut opera, O Vir magne, sed ista
Non capiet Nomen Bibliotheca tuum."

So may I say that though this building, so beautiful and complete, will be able to house and help the College of Physicians of Philadelphia, yet the name and fame of this distinguished body will forever outshine even this material monument of its now so cordially and auspiciously acclaimed success.

May you continue to possess and cherish all the gifts which Minerva and Apollo have so approvingly bestowed.

ADDRESS OF REGINALD HEBER FITZ, M.D.,

BOSTON MEDICAL LIBRARY

Mr. President, Fellows of the College of Physicians, Ladies and Gentlemen: In accepting your invitation to appear on this occasion as the representative of the Boston Medical Library, I am to be regarded merely as one of the several hundred members of that association, familiar, to be sure, with its history and one of its incorporators, but far less worthy to represent it than its librarian or one of the founders still holding the office to which he was elected at its first meeting, both of whom are among your guests of today.

The compliment you have conferred upon me I regard a call for service, as well as an honored distinction. An Associate Fellow for many years, I gladly take this opportunity of recognizing the obligation to contribute my share, however small it may be, to the celebration of this eventful occasion.

As I compare the development of your venerable body with that of the more youthful creation I am asked to represent, I am impressed with the underlying and fostering influences which have produced so vigorous a growth in each. Your College was founded by a few physicians "to advance the science of medicine, and thereby to lessen human suffering, by enlarging the avenues to knowledge from the discoveries and publications of foreign countries, and by cultivating order and uniformity in the practice of physic." When Dr. Rush, in his discourse of February 6, 1787, called attention to the advantages to be derived from this institution, he mentioned especially the establishment of a medical library. We learn that this was accomplished, and in the course of a few years it consisted "of a number of scarce and valuable

books." This contemporaneous statement loses a little of its significance, however, when Dr. Weir Mitchell, in his commemorative address at the Centennial Anniversary, states that in 1791 it was "a modest library—one case of books." But the establishment of a medical library, even in Philadelphia, was no easy task in the earlier years of the College, for in 1835 it "was in a bad condition, going to decay," and in 1843 it was "rarely if ever used."

The physicians of Colonial and Provincial Boston were none too ready to come together to lessen human suffering by advancing the science of medicine. They were much more prone to combine such efforts with a sweeping criticism of the conduct of their contemporaries. In 1736 Dr. William Douglass published an *Account of the Miliary Fever and Sore Throat of 1735-36*, which he gave "to a medical society in Boston . . . not published by way of quack bill, to procure patients and their money, as has been the practice of some in Boston." This is the first allusion to a medical society in this country, and it is not unlikely that its origin was due to the action of the Selectmen of Boston, who "desired a meeting of as many of the practitioners in physic as could be conveniently obtained," for the purpose of giving advice as to the nature and course of the above-mentioned epidemic, probably of diphtheria, which was then prevalent. As Dr. Douglass and five others were those who unanimously agreed in the advice given, it seems not unlikely that these gentlemen represented largely the medical society in Boston of 1736. Dr. Douglass was in active practice from 1736 to 1745, and further reference to this medical society appears in the *Boston Weekly News-Letter* for November 13, 1741, in which it appears that "a medical society in Boston, New England, with no quackish view, as is the manner of some, but for the comfort and benefit of the unhappy and miserable sufferers by the excruciating pain occasioned by a stone in the bladder, do publish the following case:" This society for the comfort and benefit of unhappy and miserable sufferers presumably consisted of Dr. Douglass and his friends, and did not long survive him. In an account of his life, by Dr. Jennison,[1] we

[1] Communicat. Mass. Med. Soc., 1836, v, 195.

learn that he was "held in very low estimation by many of the medical gentlemen in Boston, and his uncourtly exposure of their weaknesses served to make their resentment life-lasting. A few of the physicians in Boston and vicinity cultivated an intimacy with him until the time of his death, which dissolved all associations rationally or madly formed." Doubts were cast, later, even as to the existence of this society, for Dr. Josiah Bartlett,[1] in allusion to it, states that "a gentleman, lately deceased, whose memory included a retrospect of sixty years, and who knew the author, had no recollection of its existence. It was probably temporary, for confidence and consultation in a distressing epidemic which prevailed at the time."

The Boston Medical Library of the present day, like its predecessor of more than one hundred years ago, is the outgrowth of the action of a limited number of young physicians, interested in a common aim.

In the early part of the nineteenth century Dr. John C. Warren[2] and Dr. James Jackson[3] were the most eminent and progressive young physicians of their day in New England; of nearly the same age, energetic and active, ambitious and public spirited, thoroughly equipped with the best and broadest education of the time, they began their medical careers aided by the strongest social and family influences. About the year 1803 they formed a private society for medical improvement in connection with a few other physicians, meeting once a week, for the purpose of reading and discussing medical papers. In the course of five or six years all the members died, excepting Drs. Warren and Jackson, who continued to meet for about six years longer. I find no record of the immediate steps taken by these gentlemen in the formation of a medical library, but the Boston Medical Library, "the second social library in the town of Boston," was established in 1805. Three years later it published a catalogue of 303 books, a statement of the Rules and Regulations, and a report from the trustees to the

[1] A Dissertation on the Progress of Medical Sciences in the Commonwealth of Massachusetts, 1810, p. 12.

[2] The Life of John Collins Warren, M.D. By Edward Warren, M.D., 1850, i, 77.

[3] A Memoir of Dr. James Jackson. By James Jackson Putnam, M.D., 1905, p. 252.

proprietors, signed by Drs. J. C. Warren, Bullard, and Coffin, who were the members of the above-mentioned society. From this report I quote as follows:

"The Library receives all the periodical publications of Great Britain which relate to medical subjects, namely, the *Medical and Physical Journal of London*, the *London Medical Review*, *Nicholson's Journal of Chemistry and the Arts*, the *Memoirs of the London Medical Society*, the *Transactions of the Royal Society*, *Aiken's Annual Review*, and the *Medical and Surgical Journal of Edinburgh*. Nearly all other English medical publications made since the formation of the Library have also been obtained. . . .

"The most useful new works have been obtained from France.

"The medical publications of American physicians have been procured without any exceptions; of these are the *New York Medical Repository*, the *Philadelphia Medical Museum* and *Philadelphia Medical and Physical Journal*, *Rush's Medical Inquiries*, *Barton's Elements of Botany*, etc. All these books are firmly and handsomely bound. . . .

"The Trustees are of opinion and they think it their duty to suggest that the Library may be considerably and easily augmented. It must be confessed that an accumulation of approved old works would add much to its value and form a solid foundation for this handsome structure. This might easily be effected by donations from the proprietors of some of the books in their libraries which they have already perused. By this plan each would acquire the use of the combined contributions of his brethren. Such donations the Trustees can with pleasure acknowledge from six of the proprietors, who have contributed about forty volumes.

"Yet these gifts should be made generally before they can be important, and it may perhaps be hoped that the public and private advantages of such an arrangement will make them become general. Should this take place, we might soon behold a collection of all the medical works most important for study and for consultation; the acquisition of learning would be rendered easy, medical literature promoted, the present generation improved, and their successors inspired with emulation and gratitude."

Nevertheless, the subsequent growth of this Library was slow, as in 1816 it contained only 669 books and 95 duodecimos. The use of the books was largely restricted at first, although a proprietor could give special written orders to other persons to consult the books of the Library. In 1823, approved annual subscribers, at $10 a year, were entitled to receive books in the same manner as the proprietor, and the latter could give a standing order to a medical student for any time not exceeding three months. In 1826 there were thirty-one proprietors, and the Library consisted of upward of 1300 volumes. It was then united to the Boston Athenæum, and its proprietors were made proprietors of the latter on terms which were satisfactory to each and which provided for its continual though limited growth.

During the subsequent fifty years medical books were being added to the various collections in public institutions, State and local medical societies, medical book and journal clubs, and to the libraries of physicians. Important works were lacking, however; sets of jo rnals and periodicals were incomplete, and a prolonged s arch might be necessary to obtain the desired volume, even were it to be found in one or another of these collections.

Then came a period in the early seventies when an influx of young men, broadly trained in this country and in Europe, full of vigor, and desirous of opportunity, found a common interest in the meetings of the Society for Medical Observation. The latter welcomed the newcomers, and, among other advantages, gave them opportunity for receiving in turn the leading home and foreign medical journals, and for consulting the bound volumes of those previously received. Some of the more active and unattached of these youthful spirits formed the custom of coming together socially at the close of the stated meetings of the Society and of expressing freely their thoughts concerning men and things in Boston. The late Dr. Henry I. Bowditch, though older in years but young in enthusiasm and ready sympathy, encouraged them in the movement for the establishment of a medical library worthy of the name and convenient of access. Six of these young physicians came together at a preliminary meeting, held in his

office December 21, 1874, and in the following summer the Boston Medical Library Association was organized. Since then it has twice outgrown its domicile, has become the fourth library in size in the country, and now has a home spacious and dignified, not unworthy in situation and surroundings of the useful and valuable treasures it contains.

As the first Boston Medical Library owed its origin mainly to the efforts of John C. Warren and James Jackson, so the Boston Medical Library of the present and future must ever remain a glorious monument to the untiring zeal and constant devotion, the unselfish and self-sacrificing interest of its most conspicuous founder and its Librarian from the beginning to the day of his death, Dr. James Read Chadwick.

In the development of the College of Physicians of Philadelphia its library was at first a subordinate means to its chief object, the relief of human suffering; it would now seem that the future life of the College must depend largely upon the maintenance and expansion of its library. The Boston Medical Library, on the contrary, was constituted at the outset a corporation to establish and maintain a Library of Medicine and the Allied Sciences. It is now taking an active part in enlarging the avenues to knowledge and in cultivating order, if not uniformity, in the practice of physic. Thus the College of Physicians of Philadelphia and the Boston Medical Library meet on common ground in their effort to take their place among the benefactors of mankind, seeking nothing for themselves, but all for the race.

ADDRESS OF WILLIAM SYDNEY THAYER, M.D.

MEDICO-CHIRURGICAL FACULTY OF MARYLAND

To bring the greetings of the Medical and Chirurgical Faculty of Maryland to its older sister, the College of Physicians of Philadelphia, is an honor and a pleasure. But perhaps, after all, 'tis not as a sister that it should greet you, but rather as a child. For a large number, more than a quarter, of the one hundred and one founders of our Faculty gained their inspiration in Philadelphia from study with men who were founders or members of this honorable institution. And from that day to this, we in Maryland have ever sought refreshment from the quickening current which has flowed from the lips of your students and philosophers and poets.

Among the charter members of our Society was John Archer, who, in the year 1768, received from the College of Medicine of Philadelphia, the first medical diploma awarded in America after a course of study; and 'tis a significant fact that in the one hundred and ten years of the life of our Society nearly one-half of its honorary members ha e received their medical education in Philadelphia.

In another sense, 'tis with a feeling of peculiar pride that one enters the abode of this most distinguished and representative body. Nowhere has the physician, from the beginning, occupied so important a position in the community as here. In the past the title Doctor of Medicine has had, in many regions, an humble significance. In Philadelphia, however, from the earliest times, the social sphere of the physician has been larger and fuller than in almost any other spot in the world, and few, if any cities can point, among the annals of their practitioners and teachers and students, to so long a line of men of broad general culture, who have not only contributed to the advance of the science and art of

medicine, but have been scholars in a broader sense and true leaders of men.

Here in Philadelphia, more than in almost any other city, physician has been synonymous with gentleman and scholar. And who more exemplifies what the physician may be, how many-sided and diverse may be his interests and his influence, in science, in culture, and in letters, than your honored member, to whose fine words we listened but a few months ago in Osler Hall.

The foundation of a body such as this in 1787 is striking evidence of the general culture of the medical profession in Philadelphia over one hundred and twenty years ago. How much this College has done to elevate and uphold the standards of medicine needs no comment.

The library early became an important feature of your institution, and the influence which this admirable collection has had upon medicine, not only in this city but in the country at large, is not to be overestimated. Next to the Surgeon-General's Library, this institution is probably mainly responsible for a most honorable, and I think one of the most characteristic features of the better American medical literature. I refer to that broad familiarity shown, almost always, by the investigator with the contributions to literature of students from all parts of the world. The facilities offered for the study of the original communications of foreign authors by the accumulation of libraries such as this, and especially by the establishment of that inestimable blessing, the Surgeon-General's Library, have been of incalculable benefit to American medicine. It is largely through the opportunities afforded by these institutions, and through the foundation of the Index Catalogue and the Index Medicus, that the American student has learned so well how and where to seek the literature upon any question in which he is interested, and this knowledge and these opportunities have gone far toward delivering us from vain contentions as to priority, as well as from that medical Chauvinism which is so dangerous an enemy to the cause of truth.

At one of the earliest meetings of this College, Benjamin Rush speaks thus of the benefits which may follow its foundation: "By

stated meetings as a college we may promote inquiries and observations upon the prevailing diseases of the city. Here the timid may be encouraged and the sanguine may be taught to doubt." (What a happy phrase!) "Here the young practitioner may profit by the experience of the old, and the old by the boldness of inquiry and modern improvements of the young. Here uniformity in principle and practice in medicine will gradually insinuate themselves. Nor will the advantages of our conferences end in the acquisition of knowledge. The heart will naturally interest itself in the pursuits of the head. Here friendships will be contracted and cemented, and occasional and unavoidable suspicions or disputes may be accommodated by explanation or mediation. By these means we shall become not only the guardians of the honor of the profession, but likewise of each other's character."

What words could better describe the advantages of a college of physicians! How well have the hopes of the speaker been fulfilled!

What the physician was so early in this community, what this College has helped him to be in the century which has passed, that he is coming to be all over the world today.

Bound by no "human creed," by no blinding faith or prejudice of tradition, given over wholly to the search for truth and its application to the promotion of the welfare of mankind, no human interest is foreign to the true physician. A broad sympathy, born of a knowledge of the errors of the past and a full appreciation of the will-o'-the-wisps that beset us today, a devotion to the cause of justice and liberty, a tolerance full of pity for ignorance and the ills, moral and physical, which it bears, a hatred of superstition and intolerance, and an abhorrence of all influences which fetter or pervert the free moral and intellectual development of his fellow — these are sentiments which must animate and guide him who devotes his life to the search for truth. And so it has come to pass that the physician who, in the past, was too often the humble servant of the ruling influences in the community, social, political, religious, occupies today a position in the front rank, not only of the army of students of the natural sciences, but of every great movement for liberty, for justice, for the elevation and emancipa-

tion of the masses—careless as ever of his life in the presence of pestilence, or of his worldly reputation in the face of intrenched prejudice and intolerance. What wonder is it that men whose lives are given over to such ideals should become leaders as well as servants of mankind! What wonder is it that among them there should develop now and again those rare powers of imagination and expression which mark the great physicians whom we call poets! What wonder is it that out of our body should come a Holmes and a Weir Mitchell!

This College has been in the past one of the noblest nurseries of searchers for truth, of men who have followed consistently the wise admonition of our poet:

> "Take from the past the best its toil has won,
> But learn betimes its slavish ruts to shun.
> Pass the old tree whose withered leaves are shed,
> Quit the old paths that error loved to tread,
> And a new wreath of living blossoms seek,
> A narrower pathway up a loftier peak;
> Lose not your reverence, but unmanly fear
> Leave far behind you all who enter here!"

May it ever serve to broaden and extend the horizon of the physician, to stimulate his love of beauty and truth and justice and liberty and tolerance, to bring him nearer to his fellow man, to give to the world wise and fearless counsellors and leaders!

ADDRESS OF FREDERICK P. HENRY, M.D.,

HONORARY LIBRARIAN, LIBRARY OF THE COLLEGE OF PHYSICIANS OF PHILADELPHIA.

Ladies and Gentlemen, Fellows of the College of Physicians: It is almost twenty years since I was elected Honorary Librarian, to succeed the late Dr. James H. Hutchinson, and although, in my opinion, a eulogy of my predecessor would be as appropriate to this occasion as it would be grateful to my feelings, the time at my disposal would be far from sufficient for such a purpose. I shall, therefore, confine my remarks to the Library, and, for the reason already given—lack of time—they will have to be as superficial as my knowledge of its contents.

When I was honored with the charge of the library, in 1890, it was less than half its present size. It then contained 41,645 volumes and 12,858 unbound pamphlets. Now, according to the last report, it contains 89,220 volumes and 93,924 unbound pamphlets and dissertations. It is in the front rank of the medical libraries of the world, and second to none as a working library. I may be permitted to use this adjective in a double sense. As the term is usually employed, a working library is not only one that affords every facility for the student, but also one in which work is done—one that is largely frequented by students. As to the facilities for work I need say very little, for they are open to your inspection, but I would call particular attention to the numerous rooms for special research, in which the student may have absolute privacy, and be, practically, the owner of the room during the period of his investigation.

That the Library is largely frequented by students is proved by the fact that in 1908 there were 12,166 visitors, and 22,409 books consulted. I need say no more in proof of the assertion that this is a working library in the ordinary sense of the term. It has

proved itself, however, to be a working library in a far different sense. These books are a collection of animate objects, which have not only stimulated, but compelled progress. They forced us out of our home in the Mercantile Library, on the corner of Fifth and Library Streets, in 1854; and again they forced us out of the old Picture House, in the Pennsylvania Hospital grounds, in 1863; and, finally, they drove us, with metaphorical whips and scourges, out of our last home, about which, like the ivy that covers it, our fondest memories are entwined, and forced us to settle, like a swarm of bees, in this hive of learning. In our case, as in that of the swarming bees, it needed a metallic sound to make us settle—the sound of gold liberally poured out at our feet.

We are the slaves of these books, not their masters. No man ever mastered a book. When thoroughly imbued with its spirit, he is influenced by it for the remainder of his life. Who can say that he has mastered the Bible, or Shakespeare, or Homer, or Dante? But who has not been *captivated*, that is, enslaved, by one or all of them? We are the slaves of the book, and, through it, we have accomplished mightier miracles than were ever performed by the fabled slaves of the lamp.

We are here to stay. The bookstacks have space for 300,000 books, with ample room for extension, so that the youngest Fellow of the College need not anticipate the discomfort and expense of another removal during his lifetime.

I cannot offer you what you already possess, the freedom of this Library, but I can congratulate you and ourselves on the fact that it is contained in what is, confessedly, the finest building of its kind on either continent, and that the jewel is worthy of the casket.

CONFERRING OF ASSOCIATE FELLOWSHIPS.

PRESENTATION OF ARCHIBALD BYRON MACALLUM, M.A., BY ALBERT PHILSON BRUBAKER, M.D.

MR. PRESIDENT: Upon me has fallen the honor of presenting to you Prof. Archibald Byron Macallum, of Toronto University, Toronto, Canada, who has been unanimously elected an Associate Fellow of the College, in recognition of his services to the sciences of physiology and physiological chemistry.

Professor Macallum is distinguished as an investigator, by originality of thought, ingenuity, and accuracy of technique; as a teacher and lecturer, by clearness of ideas, logical methods of presentation, and scholarly diction; as a thinker and writer, by breadth of conceptions and philosophical interpretations of their relations to the fundamental principles of science.

For his valuable contributions to the advancement of physiology, physiological chemistry, and general biology; for his services to the cause of higher education, and for the superior worth of his personal character, he has been honored in large measure by universities and scientific associations, both at home and abroad.

It is for these reasons that the Fellows of the College desired to express their appreciation of Professor Macallum by conferring upon him the honor of an election to the Associate Fellowship. Therefore, Mr. President, may I request that you confirm the action of the Fellows by presenting him with the certificate, the visible symbol of his election as an Associate Fellow of the College of Physicians.

PRESENTATION OF OLIVER FAIRFIELD WADSWORTH, M.D., BY GEORGE EDMUND DE SCHWEINITZ, M.D.

Oliver Fairfield Wadsworth, for twenty-two years you labored with conspicuous distinction in the school of medicine of your alma mater Harvard University—first as instructor and later as professor of ophthalmology. Among the pioneers in the real ophthalmic work of this country, you have laid lines along which others have followed, secure in their markings; an investigator, you have solved difficult problems in ophthalmologic practice; a clinician, you have been distinguished for the accuracy of your observations and the keenness of your diagnostic insight; a teacher, you have sent forth your students amply equipped for the duties which confronted them, rich in the value of your instructions; an author, you have enriched the annals of American ophthalmic literature; a physician and surgeon, you have uplifted the standard of the profession and become an exemplar among the men of science.

Because of these achievements as investigator, teacher, and practitioner, I have the honor, Mr. President, representing the Fellows of the College, to request that the certificate sealing his admission into the ranks of Associate Fellows of this College shall now be conferred upon Oliver Fairfield Wadsworth.

PRESENTATION OF EDWARD GAMALIEL JANEWAY, M.D., BY JAMES CORNELIUS WILSON, M.D.

Mr. President and Fellows of the College: This institution of learning has always been jealous of the reputation of those whom it has chosen as Associate Fellows. The number has been limited, and the list contains no names but those of men who have achieved high distinction for work in medicine and the cognate

sciences, for devotion to medicine as an organized profession, and for unusual personal attainments in other respects.

I deem myself fortunate in having been selected to present as a recipient of the certificate of Associate Fellowship a man conspicuous among men in all of these qualifications, scientific physician, master clinician, learned writer, impressive teacher, wise consultant, and courteous gentleman—Professor Edward Gamaliel Janeway, M.D., LL.D., of New York.

PRESENTATION OF CHARLES LOOMIS DANA, M.D., BY CHARLES K. MILLS, M.D.

When the College of Physicians of Philadelphia elects for special honor a few out of the profession at large, its choice is determined by exceptional merit, as exemplified in the candidate whom I present.

Springing from good New England stock, a life of ever-increasing distinction has made a grateful return for an inheritance of capacity and character. Graduating at Dartmouth College in 1872, and from the College of Physicians and Surgeons of New York in 1877, he came to his profession with an unusual equipment in general scholarship and in technical attainment.

Soon choosing neurology, his position in this department of medicine was secure from the outset.

He is the author of one of the best text-books on nervous diseases and psychiatry. Some of his most notable neurological work has been in cerebral localization, in therapeutics, in legal medicine, in the establishment of new types of degenerative disease, and in the development of new ideas regarding the great functional neuroses and psychoses.

His writings stand as examples in an age of too careless and too voluminous literature.

The graces of culture, most fitting adornment of professional

men, are seen in his occasional magazine essays, in his Charaka Club contributions, in his studies of Horace, and, I might add, in such interesting and scholarly addresses as we have had the pleasure of hearing today.

Holding membership and a record of high office in some of the greatest of our medical bodies, what he brings us is reciprocity for our tribute.

Therefore, Mr. President, I have the honor to present for the certificate of Associate Fellowship in the College, Dr. Charles Loomis Dana, of New York, Professor of Clinical Medicine in the Cornell University Medical School.

PRESENTATION OF FRANK BILLINGS, M.D., BY JOHN HERR MUSSER, M.D.

Frank Billings, Professor of Medicine in the University of Chicago, sometime President of the foremost national, State, and local medical societies; attending physician and consultant to many hospitals; born of ancestry and reared in an environment which make for character, your early life was an earnest of your future career.

Beloved physician: of prophetic vision, skilled in interpretation and masterful in treatment.

Scientist: an earnest and wise seeker of truth, the torch which you carry has emblazoned the pathway for scores of young men, while your judicial mind has toned their enthusiasm. The labors of your school of internal medicine are splendid contributions to our science and our art.

Educator: the uplift of your influence is seen in the reorganized medical schools which have come under your purview in the city of your activities and felt throughout the entire field of medical education in this country.

Humanitarian: the unfortunate inmates of the charitable institutions of your adopted State have had their physical comforts increased to an extent not dreamed of, by your tact, energy, perseverance, and indomitable will, whereby they have been freed from the shackles of political bondage.

Idealist: with faith in the brotherhood of mankind, your rare powers of organization, your humane instincts, the vastness of your utilitarian conceptions, the splendid nobility of your character, are seen in the high ideals of the organization of the American Medical Association, which touches alike the community and the profession.

Recognizing the commanding features of your career, the Fellows of the College of Physicians have honored themselves by asking in one voice that you be presented to the President of the College to receive Associate Fellowship in their organization, knowing full well that you will honor it more than it can ever honor you.

PRESENTATION OF GEORGE WASHINGTON CRILE, M.D., BY WILLIAM LOUIS RODMAN, M.D.

When one, by his original work, places confrères, clientèle, and, in a broader sense, his profession and the civilized world under obligations to him, it is meet that such distinguished service should have recognition from so discriminating a body as the College of Physicians of Philadelphia.

Few in our profession have been as fertile during the past decennium, none more so, than the candidate I shall present for Associate Fellowship. He has blazed new paths in surgery, and compelled a grateful profession to follow and acclaim him as a leader. In 1897 his first monograph appeared, being an *Experimental Research into Surgical Shock*. It won for its author the Cartwright Prize, and was at once accepted as the best exposition of an intricate subject, hitherto imperfectly understood. This

classic was followed by another in 1900, on *Problems Relating to Surgical Operations, from Both an Experimental and Clinical Standpoint.* In 1901 *An Experimental and Clinical Investigation into Surgery of the Respiratory System* was published. Two years later (1903) a monograph on *Blood Pressure in Surgery*, an experimental and clinical research, was issued. In 1909, his latest and perhaps most noteworthy work, on *Hemorrhage and Transfusion*, was received, appreciated, and accepted as *ex cathedra*.

Busy as he must have been in preparing such authoritative monographs, he has found time to devise new operations, useful instruments, and to contribute many articles to current medical literature. In 1908 he delivered the oration in surgery before the American Medical Association, and was also the Mütter lecturer for this College.

Therefore, Mr. President, I have great pleasure in complying with the request of the committee, and do now present to you this distinguished surgeon, scholar, and gentleman, that you may confer upon George Washington Crile, of Cleveland, the high honor which his eminent and beneficent services so justly warrant.

PRESENTATION OF FRANKLIN PAINE MALL, M.D., BY GEORGE ARTHUR PIERSOL, M.D.

Mr. President: I have the honor to present Dr. Franklin Paine Mall, a newly elected Associate Fellow of the College.

The position of anatomy in this country has undergone a marked change during the last decade and a half. Formerly regarded as but the handmaid of surgery, today anatomy is accorded an independence commensurate with its importance as a subdivision of morphology.

In bringing about such recognition in this country, Dr. Mall has rendered conspicuous service. His investigations in detail anatomy

and especially his contributions to human embryology have won for him an international reputation.

During his career as teacher and educator he has striven with unremitting zeal to arouse in colleagues and pupils an enthusiasm for original research; and, largely through his efforts, this country now possesses two journals, of acknowledged high merit, devoted exclusively to anatomy.

Nor has it been only in the interests of his chosen science that his efforts have been directed, for his voice and pen have been used, in no uncertain vein and often in defiance of traditions, in advocating reforms affecting the broader problems of medical education.

In recognition of these services—services promoting not only American anatomy but also American medicine—the Fellows of the College have conferred upon Franklin Paine Mall the highest distinction at their disposal.

Therefore, on behalf of the Fellows of the College, I have the honor to ask, Sir, that their action be now confirmed by the certificate of Associate Fellowship.

At the conclusion of the presentation, each of the recipients of the Certificate of Associate Fellowship was addressed by the President of the College in the following words:

Duly nominated and unanimously approved by the Council, you have been elected an Honorary Fellow of the College of Physicians of Philadelphia, in evidence of which I present to you the diploma of the College signed by the President, Vice-President, the Censors and Secretary, with the seal of the College affixed thereto.

ADDRESS OF THE PRESIDENT, JAMES TYSON, M.D., ON THE DEDICATION OF THE COLLEGE.

I.

THE FOUNDATION OF THE COLLEGE.

Of the three occupations of men which are dignified by the title of profession, namely, the ministry, the law, and medicine, that of medicine has been especially characterized by a desire on the part of its members to unite for mutual improvement. While the Law has its bar associations with somewhat similar purpose, these organizations are few in number, and the synods and conventions of the Church have mainly for their object law making, disciplining, and other executive functions. On the other hand, medical societies organized for the object named have existed for centuries and have generally arisen whenever the number of physicians in a community became sufficient to form an association. Thus the *Royal College of Physicians of London*, which was evidently in the minds of our forefathers when they projected the College of Physicians, was founded in 1518, the *Medical Society of London* in 1773, the *Royal College of Physicians, Edinburgh*, was founded in 1681, the *Royal College of Surgeons, Edinburgh*, was chartered in 1505, the *Faculty of Physicians and Surgeons, Glasgow*, was instituted in 1599, *Gesellschaft deutscher Naturforscher u. Aerzte* (Leipzig) was founded in 1822, *Société de Médecine de Lyon* in 1789, *Real Academia de Medicina de Madrid* in 1732, and *Académie de Médecine de Paris* in 1820. Having been selected to represent nationalities as well as dates, it will be observed that while some of these societies have been in existence

for several centuries, others were formed more recently than our own College of Physicians.

The first effort of the kind in the English Colonies of North America appears to have been in Boston, in 1735, when an association was formed which seems never to have acquired any other name than that of a *Medical Society in Boston*, as shown in the following extract from a letter written February 18, 1735, by Dr. William Douglas, of Boston, to Dr. Cadwalader Colden, of New York:

"We have lately in Boston formed a medical society, of which this gentleman, a member thereof, can give you a particular account. We design from time to time to publish some short pieces. There is now ready for press number one with this title page." Then follows a list of papers which for some reason were never published. Several allusions were made to this society under this name during the next few years, and it continued in existence until at least 1741.

A society to which is given by Packard[1] the honor of the second place in chronological order of American Medical Societies was one entitled, *A Weekly Society of Gentlemen in New York*, to which was presented an "Essay on the nature of ye Malignant Pleurisy, that proved so remarkably fatal to the inhabitants of Huntington, Long Island, and some other places on Long Island in the winter of the year 1749, drawn up at the request of a Weekly Society of Gentlemen in New York, and addressed to them at one of their meetings, by Dr. John Bard, New York, 1749." No other mention of this Society is known.

Nor was the College of Physicians the first medical society formed in Philadelphia. The first in this city and the third in America was the *Philadelphia Medical Society*, organized February 4, 1765, twenty-two years earlier than the College, by Drs. John Morgan, J. Kearsley, Jr., Gerardus Clarkson, James A. Bayard, Robert Harris, and George Glentworth. It appears to have been limited in membership,[2] and continued in existence only until

[1] Packard's History of Medicine in the United States, Philadelphia, 1891, p. 375.
[2] Op. cit., p. 377.

November 11, 1768, when it was joined to the *American Society for Promoting Useful Knowledge*, which became subsequently the American Philosophical Society. On November 11 a number of the members of the Medical Society attended and were appointed a standing committee to consider and report upon matters relative to physic. The members at the time of fusion, in addition to those above named, were Drs. Graeme, Cadwallader, Redman, Rush, Souman, and Potts.[1]

A number of papers were published under these auspices, first in the newspapers, which were the chief media of distribution of all knowledge in that day, and also in octavo form. Dr. George Norris, in his "Early History of Medicine in Philadelphia, published by his son, Dr. Wm. F. Norris, says, "Several of these essays in book form are in my possession." He names as among them: "An Essay on the Virtues and Uses of Several Substances in Medicine that are the Natural Growth of America;" "A Dissertation on the Causes, Nature, and Treatment of Apoplexy;" "On the Dry Belly Ache, or Nervous Colic;" "On Catarrhal Peripneumonia;" and "On Consumption."

The New Jersey Medical Society, the fourth in chronological order of the Colonial societies and the oldest of existing medical societies, was organized in 1766.

A medical society was in existence in New York in 1769, and to it was given the credit of instituting the "Medical School in King's College." At least, so said Dr. Peter Middleton at the opening of this Medical School, November, 1769. It appears to have been known by no other name than *Medical Society*, and would be the fifth in order of age. There would seem to be some reason to believe that this society was continued under the name of the Medical Society of the State of New York, since on November 14, 1794, "A number of Medical Gentlemen wishing to associate for the purpose of promoting friendly professional intercourse, met at the City Hall," New York, and "after some conversation on the subject of the meeting, it was unanimously resolved that the

[1] See an extract from a letter from Dr. Rush to Dr. Morgan in 1768, in Carson's History of the Medical Department of the University of Pennsylvania, 1889, pp. 221 and 222.

present associates will, on the dissolution of the Society known by the name of the 'Medical Society' form themselves into a Society by the name and style of the *Medical Society of the State of New York*, and that they will use the seal of the same." Stephen Wickes, medical historian of New Jersey, found in the library of the New York Academy of Medicine a manuscript entitled "Minutes of the Medical Society of the State of New York," from November 14, 1794, to July 8, 1806, which would seem to confirm the suggestion above made, though it is strange that in the long interval between 1769 and 1794 there should be no other evidence of the existence of this society mentioned by Dr. Middleton. As Packard says, "there is too great a hiatus in our knowledge of the existence of a society to warrant a belief that one had remained in continuous being through all these years." I will, however, regard them as one and therefore the fifth society. In 1806 this Medical Society of the State of New York became the Medical Society of the County of New York.

The *American Medical Society*, the second of the Philadelphia societies and the sixth of all, was founded in 1773, by medical students attending lectures in Philadelphia. The meetings were held every Monday evening during the session and the society continued in existence until 1793. It consisted of Junior and Senior members, and among the latter were some of the most eminent physicians and teachers in Philadelphia. In 1790 its president was Wm. Shippen, Jr., M.D.; its vice-president, William B. Duffield, A.M.; treasurer and perpetual secretary, Henry B. Stuber, M.D.; and annual secretary, John Baldwin, A.M. Thus it will be seen that two of the officers were undergraduates in Medicine, but they were graduates in Arts. This society continued in existence about twenty years, or six years after the organization of the College of Physicians, in 1787, but the exact date of its demise does not appear. I have recently seen one of the diplomas or certificates of this society signed by William Shippen, Jr., as president, issued in 1793 to Adam Seybert, who later became a Fellow of the College.

"*The Boston Medical Society*" was organized May 14, 1780, with the object of regulating physicians' fees. The *Massachusetts Medical Society*, which still exists, was founded in 1781, the *Medical Society of New Haven County*, Conn., 1784. These three would be the seventh, eighth, and ninth in chronological order. The above named are, as far as discoverable, the medical societies formed prior to the College of Physicians January 2, 1787. In the same year were organized the Delaware and So th Carolina Medical Societies; in 1791, the New Hampshire Society; in 1792, the Connecticut State Medical Society; and in 1799, in Maryland, the Society known as the Medico and Chirurgical Faculty of the State of Maryland.

The College of Physicians, therefore, while the third of the medical societies organized in Philadelphia, was the tenth of American societies, and so far as can be learned, the oldest in existence of American societies which is not a State organization. As already stated, its prototype was undoubtedly the Royal College of Physicians of London, as the Royal Society was of the American Philosophical Society. As early as 1767 that accomplished and indefatigable physician and travelled scholar John Morgan, who two years earlier had founded the Medical School of the College of Philadelphia, later the University of Pennsylvania, began to agitate the subject of a College of Physicians, but was rather severely sat upon by one of the proprietors, Thomas Penn, who wrote to Richard Peters, February 25, 1767, as follows: "I have had a letter from Dr. Morgan and proposals for erecting a College of Physicians. I think it very early for such an establishment, and wish the faculty would not press for such a thing. I shall confer with Dr. Fotherill upon it." Suiting the action to the word, the proprietors refused to grant a charter, and the project was abandoned for the time being.

Physicians of good repute and even eminence in the mother country appeared early on the scene in the settlement of Pennsylvania. Among them were Thomas Wynne, Thomas Lloyd, and Griffith Owen. Wynne and Owen were Welshmen. Wynne

came over with Penn in the "Welcome." Lloyd and Owen arrived the same summer, as did also Edward Jones, a son-in-law of Wynne. Early in the next century came John Kearsley, in 1711, and Thomas Graeme, in 1715. Some of these became officers of the Commonwealth, associating with the office the practice of medicine or discontinuing the latter altogether. John Kearsley became the preceptor of many of the most eminent physicians of the next generation. Among his apprentices were Lloyd Zachary, Thomas Cadwallader, Wm. Shippen, Sr., Thomas and Phineas Bond, Cadwalader Evans, John Redman, John Bard, and John Kearsley, Jr. As young men grew up in the province who studied medicine, they supplemented their apprenticeship, when possible, by studies abroad. Even after the medical school of the College of Philadelphia was started, in 1765, the young men who could afford it completed their studies in Edinburgh, London, Paris, and Leyden. Thus, Morgan, Shippen, Jr., Rush, and Kuhn, after graduating at the Medical School of the College of Philadelphia, spent several years abroad and received the degree of Doctor of Medicine from the University of Edinburgh. This intercourse resulted in a close intimacy between certain of the leading physicans of London and Edinburgh and some of those of the colonies. This intimacy was interrupted for a time by the Revolution, but was quickly resumed after the war, and many Philadelphians again went abroad to finish their studies. Representing the best and most wealthy families, they were admitted to corresponding circles in England, and enjoyed the best opportunities obtainable. Correspondence was active not only between them and their teachers, but also between others. Thus, Dr. Samuel Powell Griffitts, an American student in London, wrote, August 10, 1783:

"Your idea of an American College of Physicians is what has several times occurred to me." Again the celebrated London physician, Dr. John C. Lettsom, wrote, September 8, 1783: "I think were I in Philadelphia I would not only have a Philosophical Society like our Royal Society or the French Académie des Sciences,

but likewise a medical college taking in likewise foreign members.' Thus was our College of Physicians foreshadowed.

It was not long before this shadow became substance. It is evident that, as is usual, one or more preliminary meetings had been held, that the project was talked over, and it was agreed that there should be senior and junior Fellows, as recorded in the minutes of the first meeting, January 2, 1787. Officers were appointed and a copy of the constitution presented and signed by those present. The signers were John Redman, John Jones, Wm. Shippen, Jr., Adam Kuhn, Benj. Rush, Thomas Parke, Gerardus Clarkson, Samuel Duffield, and James Hutchinson, Seniors; and William W. Smith, Andrew Ross, William Clarkson, James Hall, and William Currie, Juniors. From the constitution, which was printed a month later in the *Pennsylvania Packet and Daily Advertiser*, February 1, 1787, we learn there were to be twelve senior Fellows who alone were eligible to office, and any number of junior Fellows and associates. The seniors were to be chosen from the juniors. The junior Fellows were to consist of such practitioners of physic as were of good moral character and decent deportment and were not under twenty-four years of age. The associates were to be selected from "such persons of merit in the profession of medicine who do not live within the limits described for Fellows, that is, Southwark or Liberties of Philadelphia, without any regard to diversity of nation or religion."

Nothing is said in the minutes of this meeting of the election of officers, but at the time of the publication of the constitution in the *Packet and Advertiser* the names of the officers were published. They must, therefore, have been chosen at a previous meeting. At that time Dr. John Redman was chosen president, but did not deliver his inaugural until some time later, but no date is given and no mention is made anywhere in the minutes of the exact date of its delivery. In it Dr. Redman speaks of having accepted the appointment by a "tacit consent," but that on his return, under a strong impression of the weight both of the office and his obligation to the Fellows, he wrote what seemed to him a suitable address,

to be delivered at the next or some future meeting. At the second meeting he says he was unavoidably absent. Hence the address was delivered at a third meeting. But exactly when that third meeting was will probably never be known. It is quite possible it was a preliminary meeting, as is evident from the following extract from the Quarterly Summary of the Transactions for November and December, 1841, and January, 1842, by Dr. Henry Bond, then Secretary of the College: "The College of Physicians was instituted toward the close of the year 1786; the first meeting after its full organization was held on the second of January, 1787."

Dr. Redman was sixty-five years old when elected president of the College, and said a great deal in his inaugural about his infirmities and deficiences, but nevertheless held office eighteen years, resigning two years before he died, at the age of eighty-six, during which time the College had attained a lusty adolescence. The vice-president was Dr. John Jones, son of Dr. Evan Jones, grandson of Dr. Edward Jones, and great grandson of Dr. Thomas Wynne, who came over with Penn in the ship "Welcome." Gerardus Clarkson was the first treasurer and James Hutchinson the first secretary. The Censors were Wm. Shippen, Jr., John Morgan, Benjamin Rush, and Adam Kuhn. The constitution provided that the officers should be chosen annually, and this practice continues to the present day.

At the first meeting also a committee, consisting of Drs. Benj. Rush, Benj. Duffield, and Samuel P. Griffitts, was appointed to prepare a form of diploma or certificate of membership, and a device of a seal for the College, and another committee consisting of Drs. Wm. Shippen, Jr., Adam Kuhn, and William W. Smith, to draft by-laws, after which the College adjourned. Although only the nine senior and five junior fellows named above were present at the first meeting, at the date of publication of the constitution a list of twelve senior and twelve junior members was printed in the *Packet and Advertiser* and these have been since regarded as founders. They were as copied from the original vol. 1 of the minutes:

Senior Fellows:

John Morgan	John Redman
	John Jones
	William Shippen, Jr.
	Adam Kuhn
	Benj. Rush
	Gerardus Clarkson
	Samuel Duffield
	Thomas Parke
	James Hutchinson
	George Glentworth
	Abram Chovet

Junior Fellows:

Andrew Ross	Samuel P. Griffitts
William W. Smith	J. Morris[1]
James Hall	B. Duffield
William Clarkson	John Carson
William Currie	John Foulke
Benj. Say	Robert Harris[1]

In addition to the above names, there also signed the first constitution the following Junior Fellows, elected April 3, 1787: John Dorsey, John R. Rogers, Caspar Wistar, James Cunningham. The name of John Lynn is also found in the minutes among the Junior Fellows signing the first constitution, but is erased, for what cause is unknown. He attended one meeting, October, 1787.

The constitution provided that the meetings should be held on the first Tuesday of every month. On November 6, 1787, seventeen Fellows being present, an amended constitution was adopted, virtually the one now in force, whereby the members included only Fellows and Associate Fellows, the Junior Fellows being discontinued. The entrance fee was three pounds, Pennsylvania currency, equal to eight dollars, and the annual contribution

[1] Dr. John Morris forfeited membership in 1789 for non-payment of dues for three successive years. January 4, 1803, Dr. Robert Harris forfeited membership for the same reason, and at the same meeting Dr. Charles Caldwell forfeited membership for a like cause, but he was not a founder.

fifteen shillings, or two dollars. Through failure to pay these fees, two of the founders forfeited Fellowship.

The first meeting of the College was held in the evening in the old Academy on Fourth Street below Arch, where the University was then located. Subsequently, until 1791, it met in these premises at 4 P.M. from October to March, and at 5 P.M. from April to September.

The College was incorporated March 26, 1789, in accordance with a resolution of Dr. Morgan at a previous meeting. This is the only action of Morgan except as a donor of books, and occasional member present, recorded in the minutes after the organization. To those who are familiar with the part Dr. Morgan played in founding the Medical School of the University, this is a surprise. But he was broken in spirit and health by the unfair treatment of his country in removing him from the position of Medical Director-General, on charges of which he was ultimately exonerated, but too late. He died in October, 1789, little more than two years after the College was organized, being then only fifty-four years old. He remained a censor up to the time of his death. He was born the same year as his colleague, Dr. Shippen, Jr., who lived to be seventy-two.

The first paper read before the College was by Dr. Rush, at the second meeting, February 8, "On the Means of Promoting Medical Knowledge." At the third meeting, March, 1787, the first standing committee was appointed, that on Meteorology and epidemics. It was for a long time regarded as a most important committee, submitting annual reports, some of which were made with great care, until March, 1887, when it was discontinued. Thus was our College launched.

II.

FIRST TWENTY YEARS OF THE COLLEGE.

However interesting the history of the College during the first century of its existence, it would not be profitable to detail it on

such an occasion as this. Moreover, it has been quite fully written up for our TRANSACTIONS by one of my predecessors, Dr. Ruschenberger, in the centennial volume—the volume of 1887. The same is true of biographies of our founders, excellent sketches having been made by others, wherever it has been possible. I will, therefore, only speak of some of the more important events in our history which may reasonably be expected to be interesting.

The College early assumed a guardianship over the health, safety, and even morals of the community. As early as April 3, 1787, it appointed a committee to submit plans for establishing hot and cold baths and a botanical garden for the city. On September 4, it memorialized the State Legislature on the subject of alcohol, pointing out the harmfulness of spirituous liquors on the human body and praying that such a law be passed as shall diminish their consumption. In 1790 it memorialized the Congress of the United States on the same subject.

In 1788 it initiated action toward the preparation of a pharmacopœia of the United States, and the final consummation, in 1829, of this important work may be ascribed largely, if not exclusively, to the efforts of the College. Since that time it has taken an important part in each decennial revision.

The circumstance which made the first decade in the life of the College the most stirring and interesting in its history was the presence of the yellow fever, which first claimed its formal consideration on August 25, 1793,[1] when a special meeting was held "to consider what steps the College should take consistently with duty to their fellow citizens, in connection with the prevalence of a fever of a very alarming nature in some parts of the city." Drs. Rush, Hutchinson, Say, and Wistar were appointed to consider the subject and report the next day, August 26. On that day it was decided to meet every Monday at 4 P.M. "to confer on the treatment of the existing malignant fever."

Directions for preventing the further progress of the fever were adopted, as suggested by Dr. Rush's committee, signed

[1] This was not, of course, the first time yellow fever had prevailed in Philadelphia, this city having been visited by severe epidemics in 1692, 1699, 1741, and 1762.

by the vice-president and secretary, and a copy ordered to be sent to the mayor of the city. These directions, eleven in number, with comments on the inefficiency if not the danger of fires kindled as a means of checking the progress of the fever, and placing more dependence on the burning of gunpowder, were promptly sent to the citizens. It was further stated that "the benefits of vinegar and camphire are confined chiefly to infected rooms, and they cannot be used too frequently on handkerchiefs or in smelling bottles by persons whose duty calls on them to visit or attend the sick."

On September 3 it was ordered that the College meet every Tuesday and Friday at 4 P.M. The tragedy deepens. On September 17 Drs. Redman and Currie are the only Fellows present. After this day there is no meeting of the College until November 5, when the president submits a note in substance as follows: "October 1. The president and secretary, as well as many other members, being sick, several out of town, and the few remaining being very much engaged, the president and secretary, after exchanging letters on the subject, had determined not to issue notices of meetings." What a pregnant and pathetic paragraph was this! Alas! that such courage and devotion, such unselfishness and personal sacrifice, should have been associated with differences of opinion which led to bitterness and recrimination, to lawsuit and even personal violence, as well as the alienation of friends, and ultimately, on November 3, the resignation of Dr. Rush, who, whatever his faults, was the most eminent and most virile member of the College. There were differences of opinion as to origin and as to treatment. One set, led by Dr. Rush, held for a domestic origin, and another claimed the disease was imported. Governor Mifflin wrote to President Redman, October 30, 1793, asking whether the disease was imported, and if so by what means and at what place. If not imported, what were the probable causes producing it? What measures ought to be pursued to purify the city from any latent infection?

A committee, consisting of Drs. Ross, Parke, Currie, Carson, Foulke, B. Duffield, and Wistar, was appointed to prepare a reply

to the Governor's questions. This committee submitted a report November 12, but it was recommitted with request to have the facts authenticated. Drs. Say, Leib, and Barton were added to the committee. On November 19 the committee was discharged. They evidently could not agree. Drs. Parke, Carson, and Griffitts were then appointed to answer the Governor's questions, and on November 26, 1793, a reply was adopted to the effect that *the fever was imported in vessels about the middle of July*. Cleanliness of the streets, the use of gunpowder as a disinfectant, and of slacked lime in privy wells was recommended.

On December 2, 1794, a committee of the College was appointed to consider the defects in the health laws and suggest remedies. On the report of this committee it was resolved to memorialize the State Legislature on the subject. This was done January 26, the memorial embodying a request that "medical characters" should be appointed to assist the consulting physician of the port to prevent the spread of contagious diseases when introduced, and that they should be consulted respecting the quarantine and purification of vessels and the construction and regulation of the City Hospital.

In response the Legislature passed a new health law empowering the governor to appoint four persons, members of the College to assist the consulting physician as recommended, who were appointed the August following and were invited to meet with the Board of Health once, but another law was passed the following session excluding them "from any further share in the business."

In 1797 the pestilence again burst forth with fury, and on August 22 the College was requested by the Inspectors of the Board of Health to meet daily or as often as convenient to publish such information and offer such advice as might in their judgment check the spread of the contagion. August 26 the Secretary of the Commonwealth requested information as to the existing malignant fever. October 24 the Governor asked what measures should be used to subdue latent infection and to prevent its recurrence. All this to the College. On the other hand, the following letter,

dated Philadelphia, November 6, 1797, and addressed to Dr. Rush, speaks volumes:

PHILADELPHIA, 6th November, 1797

SIR: I am desirous to obtain, for the information of the Legislature, the most correct account of the origin, progress, and nature of the disease that has recently afflicted the city of Philadelphia, with a view that the most efficacious steps should be taken to prevent a recurrence of so dreadful a calamity. I have requested the opinion of the College of Physicians on the subject; but as I understand that you and many other learned members of the Faculty do not attend the deliberations of that institution, the result of my inquiries cannot be perfectly satisfactory without your coöperation and assistance. Permit me, therefore, Sir, to beg the favor of you, and such of your brethren as you shall be pleased to consult, to state in answer to this letter the opinion which your researches and experience have enabled you to form on the important subject of the present investigation. I am respectfully, sir, your most obedient, humble servant. THOMAS MIFFLIN.

DR. BENJAMIN RUSH.

The astute Governor evidently was not satisfied with the opinion of one party. A reply to this letter, undated, and signed by Dr. Rush and twelve others, all founders of the recently formed "American Academy of Medicine of Philadelphia," advocated the doctrine of the local origin of the fever.

The report of the College in answer to the Governor's communication was not submitted until some time later, December 24, 1797, when a committee consisting of Drs. Kuhn, Currie, Parke, Wistar, Griffitts, and James, appointed November 11, submitted a narrative of the fever, with a statement as to the best method of preventing the invasion of similar diseases in the future. It was adopted and ordered printed, January 2, 1798. The title was "Proceedings of the College of Physicians of Philadelphia, Relative to the Prevention of the Introduction and Spreading of Contagious Diseases." Printed by Thomas Dobson at the Stone-house, No. 41 South Second Street, Philadelphia, 1798, pp. 37. It contains the correspondence, memorials and other matters in connection with the Proceedings from August 25, 1793, to December 26, 1797, inclusive. The opinion of the College as expressed in the pamphlet was to the effect that yellow fever is an imported disease and spreads by contagion, an opinion directly opposite to that of Dr. Rush.

In August, 1798, the fever again broke out. A special meeting was held August 6, at which sixteen were present, called in consequence of a letter from Dr. Wistar to the president, informing

him of the existence of a malignant fever in the city. A committee was appointed to wait on the Board of Health to recommend the removal of all families between Walnut and Spruce Streets, and the east side of Front and the river; also to remove the shipping between Walnut and Spruce Streets to a proper distance. There was no meeting of the College between August 21 and November 6.

December 11, 1798, a committee was appointed to draw up a narrative of the proceedings of the College in 1793 and 1797, and the facts relative to the origin and progress of the malignant fever of 1798, with a statement of the best methods of preventing the introduction of similar diseases in the future. The result was the second report, entitled "Facts and Observations Relative to the Nature and Origin of the Pestilential Fever which Prevailed in this City from 1793 to 1797 and 1798." By the College of Physicians of Philadelphia. Printed by Thomas Dobson, at the Stonehouse, No. 41 South Second Street, Philadelphia, 1798, 1800, pp. 52.

In this pamphlet the College reiterated its previous opinion that yellow fever is an imported disease and is spread by contagion.[1]

Again, on July 1, 1799, a special meeting was called by the president at the request of the Board of Health because of the prevalence of an alarming fever. Difference of opinion again arose between the College and Board of Health. The College favored separation of the diseased from the healthy and removing the shipping which lay from South to Penn Street to a safe distance from the city, evacuating dwelling houses, stores, counting houses, and wharves as the best means of checking the progress of the disease.

The Board of Health objected to public notification, fearing that such a course might create a terror which would add to the predisposing causes of the disease if any exist, and occasion an alarm which must injuriously affect the welfare of the city and the interest of the citizens. It is evident that human selfishness worked much the same in that day as at present, and that temporizing

[1] The College published in all three papers or pamphlets on the yellow fever in 1798, 1798–1800, and 1806.

was as popular then as now. After that the College met every other evening at eight o'clock, and at a special meeting, August 21, 1799, it was decided to notify the Board of Health that a malignant contagious fever prevailed in an alarming degree.

On November 20, 1799, the Governor again asked the sentiments of the College as to the "origin and nature of the late fever." The College replied that they believed the origin and nature were "precisely similar" to those of 1793, 1797, and 1798, and that the "symptoms and progress all tend to confirm the former opinion that it is a pestilential contagious disease introduced among us by shipping," reiterating also its belief that the Board of Health should consist of persons familiar with the disease, because of the importance of its early recognition, since whatever the differences of opinion among physicians as to its origin, they have generally agreed as to the presence of the fever very soon after its appearance. The College insisted that the first step essential was the separation of the sick from the healthy; that quarantine should begin the first day of May and no ship be permitted to ascend the river until October 1.

In 1802 the fever broke out again in the neighborhood of Vine and Front Streets, and at a special meeting of the College, held July 16, it was decided that the best way to cut it short would be by an immediate separation of the sick from the healthy and the general suspension of intercourse with the infected houses. The College memorialized the Legislature to the same effect, and urged the same measures to prevent the spread of the disease. The same views were expressed three years later, in 1805, when the disease broke out in the neighborhood of Catherine and Water Streets.

In 1805 the College published "Additional Facts and Observations Relative to the Nature and Origin of the Pestilential Fever." (By the College of Physicians of Philadelphia, pp. 99. Printed by A. Bartram for Thomas Dobson, at the Stonehouse, No. 41 South Second Street, Philadelphia, 1806.) Thus, the fever prevailed, with intermissions and remissions, from 1793 to 1798, culminating the latter year, but no summer was free

from it until 1800. Two founders died of it, Hutchinson, September, 1793, and John Morris, September, 1798, and later, Hugh Hodge and William Annan, and many more, including Rush, Parke, Griffitts, and Kuhn, were very ill. As many as ten physicians died in a month, and at one time only three were able to do duty outside their own houses. Fortunately, some had become immune by previous infection.

In the summer of 1820 there occurred the last outbreak of yellow fever which visited Philadelphia. The cases occurred in the usual localities along the Delaware and were very malignant. The College reiterated its views as to its treatment and elimination.

In July, 1805, Dr. Redman resigned, and in the same month Dr. Shippen was elected to succeed him. Soon after this came a period of inactivity and indifference which contrasted strongly with the first eighteen years of the life of the College. An average attendance of 12.2, in 1788, fell to 0.7 in 1800, and to 5.0 in 1812. This average, although numerically small, was not proportionally as small as it seemed. The number of Fellows did not increase rapidly. In 1787 there were 24 founders. During twenty years between that date and 1807, 22 were added, 3 forfeited fellowship, 3 resigned, 6 died, leaving 34, or only 10 more than at its foundation, whereas it is plain that about one-fifth attended the stated and special meetings. The slowness of the growth of the College was due partly to its high ideals, but it is to be remembered also that the number of physicians in Philadelphia at that time was not large. It was thought there were about forty-six in the city when the College was organized, with some others in the adjoining districts. It is to be remembered, too, that there was strenuous rivalry. The *American Medical Society*, founded in 1773, was very active, and included among its members many Fellows of the College of Physicians, some of whom have been mentioned. It held weekly meetings from November to February. The *Philadelphia Medical Society*, the second of that name, and organized in 1789, was equally active holding weekly meetings. The Chemical Society,

instituted 1792, included some physicians, and the Philosophical Society a larger number.

Finally, in 1798, was organized the *American Academy of Medicine at Philadelphia*, by Dr. Rush and his friends, including a number of distinguished physicians who never joined the College, probably because of the influence of Dr. Rush. Dr. Physick was one of these. Dr. John Redman Coxe the friend of Jenner and exponent of vaccination in Philadelphia was another. It is said to have been organized with a view to the study of yellow fever, but it was also in evident opposition to the College of Physicians. Dr. Rush writes very quaintly of this society to Dr. Alexander under date of February 26: "I have passed this far a busy and laborious winter. My business has consisted in making additions to my lectures, in attending the hospital and many private patients, and in assisting in the forming of a new Medical Society called the Academy of Medicine. This institution will flourish. Dr. Physick is our president, Dr. Caldwell is senior vice-president, and our first publication will appear in a few weeks. It will contain the proofs of the domestic origin of yellow fever, lately presented to the government of Pennsylvania, together with some remarks on the report of the College of Physicians upon the same subject. The mint employs a few moments only of my time three or four times a week," etc., etc.

The Academy proved to be a short-lived association, the last meeting of which there is record being February 11, 1799, when officers were elected for the ensuing year.

The Medical Lyceum of Philadelphia, which was organized in 1804 and continued until 1819, must also during this time have influenced to a degree the membership and attendance on the College.

III.

FROM 1808 TO THE CENTENNIAL CELEBRATION IN 1887.

Dr. Shippen died in July, 1808, and Dr. Adam Kuhn was elected to succeed him, September, 1808, being the third president.

Dr. Kuhn died July 5, 1817 and was succeeded by Dr. Thomas Parke, July 7, 1818. At this time, thirty-one years after its foundation, the roll of the College numbered only eighteen Fellows. Dr. Parke was the last one of the founders who became president. He occupied the chair for seventeen years, until his death in 1835.

In 1821 the College was pressed for rent, it having paid none for over four years. Money was borrowed to pay the arrears, but financial stress continued through 1822 and 1823. In 1829, for the first time, the Censors reported a respectable balance of $169.42 in the treasury. In 1833, in November, the balance amounted to $208.42 which was invested, thus furnishing the first evidence of financial ease noted in forty-six years.

In 1824 the College intervened for the first time with the course of the law in appealing to the Governor of the State for respite of execution in the case of one John Zimmerman, guilty of murder. The Governor requested an examination of the man by a committee of the College, which reported him insane. The execution did not take place. I am not aware that this action has ever been repeated.

In 1824, the College of Pharmacy of Philadelphia represented that there was reason to believe that some physicians were in receipt of a royalty from apothecaries to whom they sent prescriptions, and asked the coöperation of the College in breaking up the practice. The College replied that none of its Fellows had ever degraded themselves by such a course, and hoped the College of Pharmacy would be able to dissuade its members from the practice. At the same time it invited the attention of the College of Pharmacy to the practice of prescribing over the counter by certain pharmacists. The College of Pharmacy appointed a committee to confer with the College on this matter, but the latter failed to take any part in a conference.

In 1827 the College apparently became restless over its inactivity, and resolved that each Fellow in turn, beginning at the head of the list, should at each stated meeting read an original or selected paper, which should be the subject of discussion, every person failing to comply being required to pay the sum of $1. Dr. Parke, the president, read the first paper, on the use of cold and

warm bathing. In 1829, when it was his turn to read a paper again, Dr. Parke excused himself and paid the fine of $1.

On September 4, 1827, it was resolved that the meetings, which had previously been held in the afternoon, should be at seven in the evening from October to March, and at 8 P.M., from April until September, and on December 4 the day of the monthly meeting was changed from the first Tuesday to the last Tuesday. In consequence of the change of hour, the rent was increased $6 a year because of the use of candles. On April, 1852, the day of the stated meeting was again changed from Tuesday to Wednesday, because of the interference of the College meeting with that of the Academy of Natural Sciences.

In March, 1827, a proposition was made to limit the number of Fellows to forty, but this motion did not prevail. Later, in 1833, the number of Associates was limited to forty, ten of whom were to be foreigners. In September, 1839, another effort was informally made to limit the fellowship, this time to sixty-five, but again failed. At this meeting it was decided that candidates for fellowship, instead of applying for admission, were to be proposed by three Fellows and balloted for at a subsequent meeting.

In 1832 the College, which had been meeting in the Hall of the Philosophical Society since 1791, took the first steps toward a change of place of meeting by appointing a committee to confer with a committee of the Athenæum on a proposition to erect a building for the accommodation of the several societies. This effort was unsuccessful.[1]

In 1832, when the cholera invaded the United States, the College prepared to meet it energetically, being requested April 12, by the Board of Health, to appoint a committee "to institute an impartial examination into all the facts in relation to the epidemic cholera and to report in detail the result of the investigation for the benefit and satisfaction of the unprofessional as well as the medical part of the community." This committee prepared a report, which was amended, adopted, and transmitted to the Board of Health.

[1] I have given the history of this and other efforts in this direction in an address on the "Homes of the College," at the laying of the cornerstone of the New Hall, May, 1908.

In 1835 36 another visitation of cholera occurred, and in 1848 another, by way of New Orleans and the Mississippi valley, extending as far as California. In 1854 another severe epidemic raged through the United States, for which immigration was responsible. The very serious epidemic in Europe in 1884 to 1886 again gave rise to apprehension, and in November, 1884, a committee was appointed to address Select and Common Council of the city in regard to proper measures to be taken to avert the threatened invasion of cholera the following year. A communication from the National Board of Health was read and referred to the Committee. On November 18, 1886, a special meeting of the College was held to hear an address on the subject of Asiatic cholera, by Dr. E. O. Shakespeare, who had been appointed by the United States government to study the disease in Spain.

In February, 1835, occurred the death of Dr. Parke, the president and the last survivor of the Founders. He was succeeded by Dr. Thomas C. James, who died four months after his election. Dr. Thomas T. Hewson was elected July 7, 1835. The year 1837 completed the first half century of the existence of the College.

In 1839 the College recommended to the Legislature the laying out in each district of the city of a public square with a fountain in each. Thus arose Washington Square, Franklin Square, Rittenhouse Square, and Logan Square. The College repeated this course May, 1888, urging the immediate dedication of seven small parks and future increase of small parks. This policy has been continued under the fostering care of the City Parks Association, and numerous small and larger parks scattered throughout the city attest its beneficent results. In the same line was also action by the College in 1843, when it sent to the chairman of a committee of the City Councils in charge of the matter a preamble and resolution recommending the purchase of Lemon Hill, with a view to the preservation of the purity of the water supplied to the city from the Schuylkill.

As amended in 1834, the by-laws provided a committee of three Fellows on Library and seven standing committees, as follows:

1) Theory and Practice of Medicine; (2) Surgery; (3) Midwifery; (4) Diseases of Children; (5) Materia Medica and Pharmacy; (6) Meteorology and Epidemics; (7) Public Hygiene.

It became the duty of the president or vice-president, at the stated meeting in August of every year, to assign each Fellow to one or other of these committees. Each committee was required to submit an annual report at stated times. It was the duty of the library committee to purchase books and have the care of the library as well as of papers confided to it by the College. As the number of Fellows increased, the working of the committees became cumbersome, and the by-laws were amended June, 1840, so as to require the president to appoint in June, besides a Committee on Library, one of the Fellows to report annually on each of the above-named subjects, to which was added Diseases of Women. The committees were more or less active for sixteen years, until January, 1851, when all except the Committee on Library and on Meteorology and Epidemics were discontinued. The annual reports made by the last committee were published in the TRANSACTIONS of the College until 1884, when they were discontinued.

From July 1, 1845, to 1852, the College meetings were held in the Mercantile Library; from 1852 to 1863, in the "picture house" at the Pennsylvania Hospital. In 1863 it occupied the then new Hall at Thirteenth and Locust Streets.

The College evidently looked askance upon the first effort to organize the American Medical Association. In 1845, a letter was received from the New York State Medical Society to the effect that a national medical convention, consisting of delegates from the medical institutions of the United States, would be held in the city of New York May 1, 1846, and a letter was received from Dr. N. S. Davis, requesting that delegates be appointed to represent the College. The matter was referred to a committee, of which Dr. George B. Wood was chairman, on whose report the College resolved that while it cordially approved of the proposed object, it did not, under existing circumstances, deem it expedient to appoint delegates to represent it in the convention.

Dr. Thomas T. Hewson, president, died February 17, 1848,

and was succeeded by Dr. George B. Wood, March 7, the same year.

The year 1849 was noteworthy in the history of the College from the fact that there was started the building fund by which the College was enabled to construct the Hall it has just left, and by the initiation of effort to provide a pathological museum. The steps in the collection of funds with which to construct the new Hall are ably presented by Dr. Ruschenberger in his history of the "Institution of the College," and the reader is referred to it.[1]

The first motion in the direction of a pathological museum was in June, 1849, by Dr. Isaac Parish. The by-laws were altered to provide as officers of the College a Curator and a Committee on the Museum. John Neill was the first curator elected October, 1849. The nucleus of the Museum was a collection of specimens made by Dr. Joseph Parrish. For its day the Museum grew rapidly, but it was not until it received the generous gift of the museum of Dr. Thomas Dent Mütter, along with an endowment of $30,000, that it became an important feature of the College. An idea of the value of Mütter's museum may be formed from the fact that Dr. Mütter had been offered $20,000 for it, that he had spent more than as much on it, besides much valuable time and labor.

One of the conditions of the gift of Dr. Mütter was the housing of the Museum in a fireproof building. This was rendered possible in the completion of the new building at Thirteenth and Locust streets, but occasioned some delay before all interests concerned were satisfied. By January 6, 1864, however, all preparations were completed and the Museum transferred to the College and arranged. It then consisted of 1139 specimens, 200 casts, 48 oil paintings, and 364 water-color drawings. The associated endowment provided not only for the care and insurance of the Museum, but also a salary of $300 a year for the curator, and $200 a year for a lecturer. Besides the additions by natural growth, it has acquired by purchase from time to time several valuable

[1] See Centennial Volume of Transactions of the College for 1887; also separate reprint of Dr. Ruschenberger's, "An Account of the College of Physicians of Philadelphia, 1887.

collections, including the Hyrtl collection, the Pollitzer collection, and in 1867 that of Dr. Walter F. Atlee. The collection of slides by Dr. Schmidt, of New Orleans, illustrating tuberculosis, was purchased in 1889, and in April, 1889, Dr. Henry C. Chapman presented a collection of entozoa. The purchase of books bearing on pathology was decided to be within the province of the committee on the Mütter Museum, and some valuable works have been thus obtained.

The first publication of the College may be said to the proclamation published in the *Pennsylvania Packet and Daily Advertiser*, of February 1, 1787, to the effect that the College of Physicians had been founded, adding the constitution and list of the members. The second was a eulogium on Dr. Cullen by Dr. Rush, July 19, 1790. Dr Cullen had been the professor of the Practice of Physic in the University of Edinburgh and the teacher of many of the founders when they were students at the University of Edinburgh. Hence their warm attachment and profound respect for him.

The first committee which might be called a publication committee was appointed in May, 1793. It consisted of Andrew Ross, Caspar Wistar, Samuel P. Griffitts, Michael Leib, William Currie, John H. Gibbons, Benj. Rush, and William Shippen, Jr. Under its supervision was published the first volume of TRANSACTIONS. The first three were to prepare the "copy," the second three to superintend publication, and Drs. Rush, Shippen, and Griffitts were to write a preface to the volume.

The first part of Volume I, containing among other papers an address by Rush "On the Objects of the Institution," was reported as ready for distribution August 26, 1793. The printing committee was directed to send a copy to the author of each paper in the volume, and to the medical societies of the United States and Europe, the beginning of our system of exchange, which is one of the largest and most complete possessed by any library. A pamphlet entitled *Proceedings of the College of Physicians of Philadelphia Relative to the Prevention, Introduction, and Spreading of Contagious Disease* was published in 1798. Another, entitled

Facts and Observations on the Nature and Origin of the Pestilential Fever which Prevailed in 1793, 1797, and 1798, was issued in 1800, and a third, entitled *Additional Facts and Observations Relative to the Nature and Origin of the Pestilential Fever, by the College of Physicians*, was published in 1806. Dr. Wistar's "Eulogium on Dr. Shippen" was delivered in 1809 and published by the College in 1818.

After a period of inactivity extending over several years, measures were adopted in October, 1841, to publish quarterly a summary of the TRANSACTIONS, and a publication committee was appointed. Between 1841 and 1850 three volumes were thus issued under the direction of the Committee on Publication. Agreement was made with a firm of publishers to print and sell the work, and a new series of the summary of the TRANSACTIONS was begun in 1850, and continued to the end of 1857. Then, to save expense, an arrangement was made with the proprietor and editor of the *American Journal of the Medical Sciences* to publish, free of cost, the written and verbal communications and the abstracts of discussions, and to supply a sufficient number of extra copies for the use of the College. Under this arrangement a new series was started and continued until the completion of the fourth volume, in 1874.

In the latter year the contract with the *American Journal of the Medical Sciences* was annulled and the College resumed the publication of its TRANSACTIONS. The first volume of this, the third series, was published in 1875, and the thirtieth in 1908. In 1885 the publication committee was $822.33 in debt, and, in view of the desperate situation, a proposition to accept an offer of the *Medical Times* to publish the TRANSACTIONS without expense to the College was considered, but through the generosity of Dr. Da Costa, who was then president, the debt was paid and the publication continued by the College itself.

Between 1864 and 1887 the life of the College was not signalized by striking events. Dr. Ruschenberger succeeded Dr. Wood as president in 1879.[1] Dr. Stillé followed Dr. Ruschenberger

[1] This year it was enacted that no Fellow shall be eligible to the office of president more than five years in succession, and in 1882 tenure of office was limited to three years.

in 1883, and Dr. Samuel Lewis served for a short time in 1884, resigning on account of ill health. Dr. J. M. Da Costa was chosen for the unexpired term and reëlected in 1885. Dr. Mitchell was elected in January, 1886, and again in 1887 and 1888.

The library and museum both grew rapidly, and it was evident that more space would be required for both before long. This stimulated the Fellows to prepare for such requirement, and on January 6, 1875, a committee was appointed to devise a plan for collecting a building fund, which was called the "building extension fund." The committee reported April 7, 1875, proposing that all entrance fees and any annual surplus which the College could afford should be appropriated to this fund, and that subscriptions, donations, and legacies to it should be encouraged. This was adopted. On December 1, 1875, $400 was transferred from the treasury of the College to the fund, and on March 3, 1883, Dr. Da Costa gave the first personal subscription of $1000; and a committee was appointed to solicit further contributions. This fund grew rapidly, and in the course of a few years became sufficient to enable the College to complete the third story of the Hall, providing, it was thought, for the growth of the museum and library for many years to come. The extension was begun May 27, 1885, and finished May 31, 1886.

The Mütter lectureship gave much concern. By the terms of the bequest, once in three years a lecturer was to be appointed who should give a course of not less than ten lectures each year on some subject connected with surgical pathology. Dr. John H. Packard was the first lecturer, and gave a course upon "Inflammation," in accordance with the conditions, but after him it was found difficult to secure competent lecturers. Several partial courses were given, and some appointed resigned before giving a single lecture. By agreement with the executors of Dr. Mütter's will, modifications were made in the conditions which permitted the delivery of one course of lectures triennially, and that the lecturer should receive the whole compensation for three years. In this way several more courses were secured, eight courses of ten lectures in all, but even this arrangement fell through subsequently, and

at present, by resolution, June, 1901, it was made an annual lectureship, the remuneration to be $200.

The year 1882 was characterized by the establishment of a directory or bureau of registration for nurses. While such a function might at first be thought beneath the dignity of a medical society of the importance of the College, a moment's reflection must convince one that the purpose is legitimate and directly in a line with the treatment of disease and alleviation of suffering. On the other hand, there can be no doubt that the importance and dignity of the College gave at once a character and respectability to the movement which did much to secure its immediate success. Organized in 1882 by a committee of the College, aided by a number of influential women of the city headed by Mrs. Weir Mitchell, the Directory is continued under the management of this committee, known as the Committee on the Directory for Nurses. Its members are annually elected, and it is assisted by four ladies selected by the committee. The Directory has not only been of service to the community in supplying promptly efficient nurses from those registered, but it has also aided the latter in securing employment, and has paid into the treasury of the College many thousands of dollars which have been devoted to increasing the library.

IV.

THE CENTENNIAL CELEBRATION AND SINCE.

The College in its infancy and for some time afterward was very poor. It was often in arrears with its rent, and once had left it unpaid for four years. On this account social entertainment attracted little attention until November, 1877, when the Council was directed to consider whether it was advisable for the President to give an annual reception at the expense of the College. The Council reported that the state of the treasury alone rendered such a course inexpedient. In February, 1883, Dr. Weir Mitchell presented $5000, subsequently increased to $7000, to establish

an entertainment fund. This generous gift and its purpose was followed by the appointment of an entertainment committee, which has been called upon to exercise its function on several occasions. The first was a reception given to the medical members of the American and British Associations for the Advancement of Science, September 8, 1884. Under the direction of the committee a dinner was given by the College, April 14, 1886, at which a loving cup, presented by Mrs. Weir Mitchell, was used for the first time. A reception to the State Medical Society followed in June, 1888, since which the Fellows have dined together in their own Hall several times.

Thus we approach the most important event in the history of the College after its organization, namely, the Centennial Anniversary, celebrated Monday and Tuesday, January 3 and 4, 1887. The celebration may be said to have commenced with the arrival of invited guests on Sunday, January 2, the actual anniversary. The day was bitterly cold, and is especially associated in my mind with the presence of that gentle and accomplished physician, R. Palmer Howard, then Professor of Medicine in McGill College, Montreal, who was my guest and whom I took in the afternoon to old St. Peter's church on Pine Street, where lies buried John Morgan, one of our most brilliant and accomplished founders, so that a visit to the church seemed natural and appropriate. In the evening our guests were entertained at tea and social visits were exchanged.

On the next morning the ground was covered with snow, so that Philadelphia appeared clad in gala dress for the occasion. In the evening there were dinners to our guests at the homes of the Fellows, and at 7.30, at Association Hall, a commemorative address by our beloved president, Dr. Weir Mitchell, who reviewed the lives of the founders and of some of their predecessors, bringing out the traits and characteristics of each. I know of no better short sketches of these worthies than those then read by Dr. Mitchell. Following the address was a general reception to the public and Fellows at the Hall of the College, where was also

displayed a loan collection of portraits of eminent physicians and rare objects of professional interest.

On Tuesday, January 4, the second day, a special meeting of the College was held at noon, when Prof. Alfred Stillé delivered an address entitled "Reminiscences of the College," but which in connection with the commemorative address of Dr. Mitchell, constitutes a good condensed history of the College from its foundation to the centennial celebration. On the same occasion certificates of associate fellowship were presented by the President to eleven eminent confrères from different sections of the country. Each presentation was preceded by appropriate remarks referring to the special attainments of the proposed Fellow. Then followed an address of welcome to the new Associates, by Professor J. M. Da Costa, and succeeding this a luncheon. Alas! all except two of the associates have gone to their long homes. All are names over which we who knew them love to linger. They are Robert Palmer Howard, of Montreal; William H. Draper, of New York; George Cheyne Shattuck, of Boston; Nicholas Senn, of Chicago; T. Gaillard Thomas, of New York; James T. Whittaker, of Cincinnati; David W. Yandell, of Louisville, Kentucky; John C. Reeve, of Dayton, Ohio, and Hunter McGuire, of Richmond, Virginia. Only Dr. Cheever and Dr. Bowditch remain.

In the evening 120 Fellows, Associates, and guests of the College sat down to dinner in the banqueting hall of the Union League. There were toasts and appropriate verses, and the loving cup was passed amid much rejoicing and congratulation that the College had rounded its first century under such favorable circumstances. Death, too, has dealt harshly with those of the company who spoke at the dinner. Agnew, who replied to the toast "The Fellows of the College," Gaillard Thomas, who spoke for the "Associate Fellows," William Pepper, who replied for "The Physician," Ashhurst, for "The Surgeon," Parvin, for "The Obstetrician," George Cheyne Shattuck, an Associate and the son, and father, of an Associate, who toasted "The College of Physicians," and Henry Hartshorne, who read a poem entitled "The Old and the New Physic," have all gone. Only Billings, who spoke for "The

Medical Societies of America," and Mitchell, who read "Commemorative Verses," survive.

The occasion also marked the completion of the *then* new College Hall at Thirteenth and Locust Streets, by the addition of the third story at a total cost of $67,256.50, including the site, which cost $14,408. This sum, even so late as 1887, was thought to be very large, and the then new Hall was put in strong contrast with the modest room in Fourth Street where the first meeting was held one hundred years earlier. Speaking of the trustees of the building fund as constituted in 1849, when a small sum in the treasury of the College was devoted to this purpose, Dr. Stillé said, in his centennial reminiscences, "To their wise and prudent management we owe the foundation, and much more than the foundation, of the *great* building in which we are this day assembled." Yet the total investment is insignificant as compared with what has been expended for this, our latest home, appointed as no building for a like purpose ever was. Short as has been the interval since our centennial celebration, I do not believe that our seniors of the latter day had any better idea of the changes a quarter of a century would bring about than had Morgan, Shippen, Kuhn, and Rush, in their day, of the possibilities of the coming century.

The College of Physicians did not die with the centennial celebration. Its work stands out less conspicuously in some respects than in the old days because it is now one of many instead of a few societies existing for many years after its foundation. Less frequently called upon to express its opinion and render aid to the city, State, and nation, it has nevertheless continued its suggestions and criticisms when they seemed opportune, and they have been generally received with consideration and respect, while the College has been of infinite service in extending the treasures of its library to the thousands of physicians and students whose researches and writings would have been impossible without its help.

One of the most important functions of the College developed in this period is the stand it has taken against encroachment on the right to use, humanely, animals for investigating the action of

medicines and determining the causes, prevention, and cure of disease. As early as February, 1885, the College memorialized the Legislature on the "antivivisection bill" which was before that body. Its efforts were successful in preventing the passage of the bill. In April, 1886, a committee was appointed charged with the protection of the right of scientific research, with Dr. H. C. Wood as chairman. The vigilance of this committee was exercised for some time in behalf of the interest of science, and although it is no longer maintained, its work has been continued by resolution, memorial, or the acts of specially appointed committees. Almost every biennial session of the Legislature has called for efforts in the direction of its purposes, and they have all been successful. The College also petitioned the national government, when several years ago legislation against experimental medicine was attempted but thwarted.

The same broad humanitarian purpose was shown in its approval, by resolution, February, 1887, of the action of the United States Senate in appropriating $10,000 toward the expenses of investigating the etiology of yellow fever in South and Central America. In line with this action was a resolution of the College, January, 1893, urging the passage of a bill by Congress, allowing the widow of Dr. Walter Reed, who fell a victim to his zeal in the study of the cause of yellow fever, a pension of $4000 a year. Also a resolution, January, 1903, asking the President of the United States to grant the amplest authority to the medical officers in charge of the sanitation of the Isthmathian Canal construction, and urging that a medical officer be made a member of the Commission, to be appointed by the President to conduct the affairs of the proposed canal. Whatever may have been the influence of the College in securing such appointment, the action has been more than justified by the brilliant and satisfactory results obtained by our Associate Fellow, Dr. Wm. C. Gorgas, in the administration of his duties as sanitary officer.

The subject of quarantine has at all times received the interested attention of the College, beginning with the efforts in this direction when the city was battling with the yellow fever from 1793 to 1798.

Unfortunately, diverse interests as well as the changing and antagonistic views of those claiming special knowledge on this subject have often rendered efforts nugatory. These unsatisfactory results have been further favored until lately, and to some extent at the present time, by our ignorance of the precise causes of certain infectious diseases. After yellow fever, cholera claimed attention, first in 1832, and later, in October, 1887, when a committee was appointed to secure concerted action on the part of the medical societies of the land in obtaining a uniform and efficient system of national quarantine against contagious diseases, and especially against cholera, for all exposed ports.

In December of the same year a special meeting was held to consider the address of the committee on Cholera above referred to. The address was approved and ordered sent to these societies. In February, 1893, resolutions were adopted advocating international quarantine in all frontiers and the establishment of a national department of health, which were forwarded to the Congress of the United States.

In May, 1893, a quarantine board was created by the Legislature of the State of Pennsylvania for the administration of State quarantine on the Delaware River, providing also for representation of the College. The president appointed to this service our Fellow, Dr. Richard A. Cleemann, who continues to discharge it to the satisfaction of the College.

April, 1888, the College continued its role of protector of public safety by passing a resolution protesting against the use of water gas as a mixture with coal gas for illuminating purposes in greater proportions than 10 per cent. In May a letter was received from the Mayor promising to give careful attention to this request. Apparently this promise was ineffectual, for many lives are sacrificed annually by this agent.

The College has always been ready to render, to the extent of its ability, aid to members of the profession who have suffered in public calamity. Accordingly, in June, 1889, at a special meeting, a committee was appointed to act in coöperation with one from the Philadelphia County Medical Society for the relief of the sufferers,

and especially medical sufferers, by the Johnstown flood. Response was liberal in money and in personal service by volunteers, who hurried to the scene of the disaster. In May, 1906, the College coöperated with the County Medical Society in similar efforts for the immediate relief of the physicians of San Francisco succeeding the earthquake. In June it was ordered that duplicate volumes from our library be presented to San Francisco medical libraries at the discretion of the library committee.

The College has never taken a very active part in influencing medical education, though an interesting event in its early history may be mentioned in this connection. At a special meeting as early as March 10, 1794, it was announced that the chairman of a committee of the House of Representatives, charged with the preparation of a bill "to regulate the practice of physic within the State," had asked the assistance of the College. Accordingly the College recommended, March 14, that, excepting graduates of the University, all applicants for license to practise within the State should be examined by persons appointed by the College for this purpose, under penalty for non-compliance; also that apothecaries should be examined for license. A bill embodying this and other provisions was introduced into the Legislature a couple of weeks later, March 24, 1794, but it was laid on the table; and although a motion to bring it up on second reading, Monday, March 31, prevailed, it was not read, and no further reference to it has been found.

In February, 1891, a committee was appointed to represent the College before the Legislature in advocacy of a bill to establish a State Board of Medical Examiners and Licensers, and in opposing a bill providing a State Board of Medical Education. The bill establishing a State Board of Medical Examiners was passed, and has been of great service in advancing the standard of medical education.

In January, 1892, Dr. Mitchell was again elected president, succeeding Dr. Agnew, and reëlected in 1893 and 1894.

In 1893 the College, desiring to increase the opportunity for the reading of papers often encroached upon at the monthly meetings

by a pressure of business, voted to establish sections representing the different branches of medicine, to meet as often as deemed necessary, in addition to the stated monthly meetings of the College. Under this resolution were formed sections on surgery, orthopedic surgery, ophthalmology, otology and laryngology, gynecology, general medicine, and medical history. They have been variously successful, that on ophthalmology especially so. The same is true of otology and laryngology. That on general medicine is not as successful as it should be; due in part to the fact that there are many other society meetings at which medical papers and reports of cases are read. The sections on surgery, orthopedic surgery, and gynecology have been discontinued.

In January, 1895, Dr. Da Costa was reëlected president, at the end of Dr. Mitchell's second administration of three years, and reëlected in 1896 and 1897.

In January, 1898, Dr. John Ashhurst became president, and was reëlected in 1899.

In January, 1900, Dr. W. W. Keen was chosen president, and reëlected 1901. Dr. Keen's administration was characterized by unusual success in increasing the endowment and growth of the library. An additional endowment of $50,000, largely through Dr. Keen's personal efforts, was secured.

In January, 1902, Dr. Mitchell announced from Mr. Andrew Carnegie the gift of $50,000 toward the construction of a new hall, conditioned on a like sum being raised by subscription.

Dr. H. C. Wood became president in January, 1902, and was reëlected 1903. His administration was characterized by the initiation of active measures toward meeting the demand for increased space to accommodate the rapidly growing library, and at a special meeting held January 21, 1903, he exhibited plans of alteration and enlargement of the old Hall, as we shall now call it. At the same meeting a committee was appointed to consider plans. From this time forward were announced numerous contributions to the building fund, and Mr. Carnegie's conditions were soon met.

Dr. Arthur V. Meigs was elected president in 1904, and reëlected

in 1905 and 1906.[1] His administration was characterized by much activity in the settlement of the question of removal to a new site for the proposed new Hall.

In May, 1903, the question of removal and the securing of an option on certain lots was referred to a committee, which at a special meeting, held May 29, recommended the purchase of a lot on Twenty-second Street below Chestnut, for $80,000. This was authorized. In November a committee on plans was appointed, which reported April 6, 1904, and was then replaced by a building committee, under which, with additions, the new Hall we now inaugurate has been constructed.

At a special meeting, March 30, it was decided to remove to the Twenty-second Street lot. In May, 1906, the College, having in the meantime heard the report of a minority committee opposed to removal, and having been in negotiation for several lots rejected for various reasons, reaffirmed its intention of erecting a new Hall on Twenty-second Street, and the building committee was directed to proceed with the duty assigned to it in the matter of plans and estimates to be presented at the October meeting. Stewardson & Jamison were selected architects, ground was broken January 30, 1908, and the corner-stone was laid with suitable ceremonies April 29, 1908.[2] It is finished today, November 10, 1909.

Having considered some of the important events in the history of the College, I may be permitted, in conclusion, to select a few

[1] It was on April 6, 1904, that the College adopted a *resolution* to the effect "that a Building Committee of Six (6) be appointed, to consist of the President, who shall be the chairman, and five other Fellows appointed by him."

Under this resolution the committee included:

The President, Dr. A. V. Meigs, Chairman,
Dr. James Tyson, Dr. William Thomson,
Dr. J. C. Wilson, Dr. William J. Taylor,
Dr. George McClellan.

On May 4, 1904, the College voted that an additional member of the committee be appointed by the President, and Dr. J. K. Mitchell was appointed.

Dr. Meigs' term as President expired at the January meeting, 1907, leaving a vacancy which was filled, on February 6, 1907, by the appointment of Dr. G. E. de Schweinitz by the President (Dr. Tyson).

On April 3, 1907, the Treasurer, Dr. R. H. Harte, was added to the committee.

Dr. Thomson died on August 3, 1907, and Dr. F. P. Henry was appointed in his place.

[2] See Transactions of the College, third series, vol. xxx, appendix

links from the chain of events which bind the past to the present and which have more or less shaped its course and determined its auspicious present: *First*, a foundation following the example of the best type of the English medical society; *second*, founders, twenty-four in number, most of them trained in the best medical schools in Europe, succeeding the best obtainable education at home; *third*, experience either in the field or practice at home during an eight years' war characterized by privation and hardship which broadened the knowledge, increased the skill, and developed the character of those concerned in it; *fourth*, a baptism of pestilence and death, which, by the difficult problems it raised, disrupted friendships and endangered the existence of the College itself; *fifth*, through patience of surviving founders and other members added, with the lapse of time, a revival of life, a new growth of strength, and development of service until through its various functions the College has become a great power for the increase and dissemination of medical knowledge and for inspiring the higher aims of the medical life.

At the time the College was founded medical science was overweighted with theory, and the theories of Stahl, of Hoffman, of Boerhaave, of Curren, of Brown, of Brussais and others were much discussed, with the usual vapid results of theoretical speculation, and it is perhaps fortunate that opportunities for writing were limited by distance from what were considered the fountain heads of medical learning of that day, and by the difficulties which surrounded printing and book making in general. It is on this account, perhaps, that our earlier TRANSACTIONS, though not copious, were of a more practical character than those of the societies of other English-speaking communities of the day, comparing well with such Transactions and those of other foreign countries.

It is gratifying also to note from the biographical sketches of our founders and their immediate successors that pecuniary emolument played a minor role as a motive in their practice, that personal danger was ignored, that relief to the suffering of their

fellow citizens was their first aim, that they lived, in a word, up to the motto of the College:

NON SIBI SED TOTI.

NOT FOR ONE'S SELF BUT FOR ALL.

V.

THE LIBRARY.

As early as June 3, 1788, a committee was appointed to report a plan for the formation of a library, whose report was laid on the table July 1. On August 5, however, it was resolved "that the several members of the College be requested to send to the secretary such books as they were willing to present to the College." Dr. John Morgan was the first liberal respondent, presenting twenty-four volumes in December, 1788, and others in January, 1789. On March 3, 1789, the same committee reported a plan of collecting, buying, storing, and lending the books, which was adopted. Almost immediately the growth of the library, when the day and times are considered, was phenomenally rapid. Among the other early liberal contributors were Dr. William Shippen, Dr. John Morris, Dr. John Jones, Dr. Benjamin Rush, and Dr. Parke. The first catalogue was completed January 5, 1819, after some books were found missing. For a time after this the growth of the library was slow, and in 1836 there were only 291 volumes in addition to a number of unbound pamphlets. In 1834 a standing committee on the library was created, the chairman of which was regarded as librarian, and the office of librarian was not created until 1854. In 1835 a committee reported the library in bad condition, and was instructed to take steps for its preservation. Between 1819 and 1843 very few volumes were added, and the books were rarely used. Succeeding 1843 the growth became more rapid, culminating, in 1858, in a gift of 1265 volumes from Dr. Thomas F. Betton, including many rare and important works. In May, 1859, the library was ordered open one evening in the

week. In December it contained 4000 volumes, besides pamphlets and theses.

But the real growth of the library began with the munificent gifts of Dr. Samuel Lewis, the first of which was made in February, 1864, when he gave more than 2500 volumes through the chairman of the Library Committee, Dr. Alfred Stillé. This gift became the nucleus of the Lewis Library, which contained at the end of 1909, 13,536 volumes.

On March 4, 1868, was started the Library Fund by a donation of $445.90 from the Philadelphia Medical Society, increased by the College to $500 and ordered invested. At his death, in 1879, Dr. George B. Wood gave $7581 to the Library for purposes other than the purchase of books. In November, 1880, Dr. S. Weir Mitchell gave the first $1000 toward the Library fund, which he subsequently increased to $5000. In 1871 a journal club was formed, which annually contributes to the Library sixteen periodicals.

A card catalogue was commenced in 1881 by Miss Emily Thomas. In 1884 Dr. Alfred Stillé gave 695 volumes. In April, 1884, the S. D. Gross Library (5128 volumes) of the Academy of Surgery was deposited, with the understanding that it should become the property of the College when the Academy should be dissolved. In the same year was deposited the library of the late Dr. H. Lenox Hodge, known as the Hodge Collection, and later became the property of the College as a gift from his son. In 1886 Dr. I. Minis Hays presented 901 volumes, and Mr. George I. McKelway 166 volumes. In 1886, also, Mrs. J. F. Weightman presented 512 volumes to the library, of which 351 were new and dealt chiefly with ophthalmology. In 1887 Mr. William Weightman gave $1000, the interest of which was to purchase books on ophthalmic surgery, to be added to the collection given by the widow of Dr. Weightman.

In 1886 the John S. Parry library and the library of the Obstetrical Society were contributed. In 1887 the library of Dr. Archer N. Randolph, 466 volumes, was presented to the College. In 1887, by sale of duplicates and special books belonging to the S. D.

Gross Library and the general library, $786.65 was raised, of which $640.75 was given to the Gross library and $145.90 to the obstetrical library.

In 1890 Mrs. Deborah K. Rodman donated to the College $5000, to be paid within five years, in memory of her late husband, Dr. Lewis Rodman, the income of which was to be used for the purchase of books.

In 1894 Clement A. Griscom presented $5000 to constitute the John D. Griscom fund. The same year were added 796 French and German dissertations and 377 volumes of foreign journals, while the files of thirty-three of the most important French and German periodicals were completed. Also, in 1896 and 1897, through the liberality of Dr. J. M. Da Costa, there were purchased 293 volumes needed to fill the gaps in the files of valuable foreign periodicals. In 1899 Dr. George Fales Baker presented $5000 to be known as the Henrietta Rush Fales Baker Library Fund, and Mrs. Elizabeth B. Judson $1000, as the Oliver A. Judson Fund, of which the income was to be expended for the purchase of books relating to preventive medicine. Then followed rapidly subscriptions by Luther S. Bent, of $1000; Wm. T. Carter, $5000; Mrs. William F. Jenks $7000, transferred from the Wm. F. Jenks Prize Fund; Wm. V. and John M. Keating, $1000; W. W. Keen, $5000; Caspar Wistar, $5000; Alice Gibson Brock, John H. Converse, Wm. W. Frazier, Charles C. Harrison, and Sara Kobel, each $1000, with numerous smaller sums. Many of these were obtained by Dr. W. W. Keen, through whose efforts the Library fund was raised to $50,000 by July 1, 1900. The entire Library fund, up to November 1, 1909, amounted to $65,332, not including the George B. Wood bequest of $7581 for purposes other than the purchase of books (salary of librarian, etc.).

Other noteworthy gifts in books were a large portion of the libraries of Dr. Alfred Stillé, Dr. J. M. Da Costa, and Dr. John Ashhurst, Jr., all of whom died in 1900. Almost the entire library of Dr. Stillé had been given during his lifetime to the Lewis Library before Dr. Lewis's death, in 1890. It included many rare and valuable books.

Dr. Da Costa's library was received in 1900. It included 2466 books, among which were many elegantly bound volumes. Fifteen hundred volumes were selected from the library of Dr. John Ashhurst, many of which were rare and all valuable.

In 1900, also, were received 6963 theses and inaugural dissertations, and there was arranged, chiefly through the efforts of the president, Dr. Keen, an exchange with six universities, French, German, and Spanish. These exchanges have been increased through Dr. Keen's efforts, in 1908, to twenty-six universities. Nine hundred and forty-eight inaugural theses were received in the year 1907, and through the efforts of Dr. W. W. Keen, Dr. Wm. Osler, Dr. A. J. Magnin, and Dr. Louis Landouzy, Dean of the Paris Faculty of Medicine, it has been arranged that we receive in exchange for our TRANSACTIONS the forty or fifty volumes of the Paris theses published each year. With a view to further completing our files of the Paris theses, by an appeal to Fellows there was raised a sufficient sum to complete our files from 1882 to 1907, more than 850 bound volumes. From delayed shipment, however, these volumes did not arrive in time to be included in the accessions to the Library reported by the librarian for 1908. They will, however, be included in the report for 1909.

In 1901 was secured, through subscriptions by Dr. S. Weir Mitchell, Dr. George Fales Baker, and Dr. John K. Mitchell, the library of the late Dr. J. Stockton Hough, a unique collection numbering 3247, and 2070 pamphlets, of which 1500 volumes and 1030 pamphlets were retained, the remainder being sold to the University of Pennsylvania for $1500.

In 1902 the ophthalmological library of the late Dr. Wm. F. Norris, consisting of 1177 volumes, and constituting one of the most valuable collections of works on ophthalmology, was presented by his family. In 1903 Dr. George W. Norris presented three volumes containing the collection of colored eye grounds made up of the original drawings and notes of Professor Jaeger, of Vienna, from which the well-known Jaeger atlas was produced, and purchased by his father, Dr. Wm. F. Norris, for $2400; also a volume containing the collection of ophthalmological draw-

ings from cases seen in the practice of Dr. Norris from 1873 to 1901.

In 1904 the library of the late Dr. Thomas M. Drysdale, 958 volumes, was received.

In 1905 the Board of Managers of the Episcopal Hospital presented its library of 1982 volumes, and Dr. J. V. Ingham gave 548 volumes.

In 1907 the late Mr. John Lambert left in his will $5000 to the Library as a memorial to his cousin, Dr. W. F. Norris.

The Elizabeth K. Newcomet fund of $1000 was contributed by her son Dr. Wm. S. Newcomet in 1908.

Dr. Keen's unceasing efforts brought further fruit in the purchase abroad, in 1908, of thirty-three rare and valuable medical works, of which twenty-one were incunabula (printed in the fifteenth century), and two, though not incunabula, are of great value. They are a copy of the works of Avicenna in Arabic text (1593) and a fine edition of photographic fac-simile of the Dioscorides Codex, in two large folio volumes, published in Leipzig, 1906. Dr. Keen was aided in the purchases by the liberal subscriptions of a few friends of the College.

Mention should be made of the Nurses' Directory as a liberal source of revenue to the Library. Established May 15, 1882, it has not only been a great boon to the community in promptly furnishing efficient nurses, but has also contributed to the College during the years 1900 to 1907, inclusive, over $15,000, all expended in the purchase of books.

The total number of bound volumes up to November 1, 1909, is 81,018; General Library, 63,890; Lewis Library, 13,536; S. D. Gross Library, 3375; Obstetrical Society Library, 217. There are also: Unbound Reports and Transactions, 8202; unbound Theses and Dissertations, 23,711; unbound Pamphlets, 70,213.

Between 2000 and 3000 volumes are purchased annually with funds of the College, and many are donated by authors, publishers, and friends of the College.

BENEDICTION, BY THE RT. REV. OZI W. WHITAKER.

Almighty God, who calledst Luke the beloved physician, whose praise is in the Gospel, to be an evangelist and physician of the soul, may it please Thee that by the wholesome medicines of the doctrine delivered by him all the diseases of our souls may be healed, through the merits of Thy Son, Jesus Christ, our Lord. Amen.

Almighty God, who art the giver of every good and perfect gift, and from whose inspiration all our best desires and noblest purposes do spring, we heartily thank Thee that Thou hast enabled Thy servants to complete the erection of this new Hall of the College of Physicians, in fulfilment of their long cherished aim; and we humbly beseech Thee graciously to accept the dedication of this house for the beneficent uses for which it is designed. May it ever be so used as to promote the love of sound learning, the progress of medical science, the increase of skill in the art of healing, the prevalence of health of both body and mind, the exercise of kindly fellowship, the welfare of mankind, and the honor of Thy holy name, through Jesus Christ, our Lord. Amen.

The God of Peace, Who brought again from the dead our Lord Jesus Christ, that great Shepherd of the sheep, through the blood of the everlasting covenant, make you perfect in every good work to do His will, working in you that which is well pleasing in His sight, through Jesus Christ, to whom be glory for ever and ever. Amen.

DINNER OF THE COLLEGE OF PHYSICIANS OF PHILADELPHIA ON THE OCCASION OF THE DEDICATION OF ITS NEW HALL.

November 10, 1909. The Bellevue-Stratford.

MENU

Cape Cod Oysters
Celery

Puree Argentine

Almonds Relishes Pecans

Planked Bass Bellevue
Potatoes Hollandaise

Roast Young Lamb, Mint Sauce
Green Peas

Pennsylvania Quail

Lettuce and Tomato Salad

Camembert and Roquefort
Toasted Crackers

Fruit and Flower Ices
Fancy Cakes

Coffee

Martinis Krug Brut Cigarettes
Liqueurs Cigars

TOASTS

"THE OLD COLLEGE AND THE NEW"

Dr. S. Weir Mitchell

"LIBRARIES AND THEIR FOUNDATIONS"

Mr. Andrew Carnegie

"THE COLLEGE LIBRARY AND ITS TREASURES"

Dr. W. W. Keen

"THE COLLEGE AND ITS CIVIC RELATIONS"

Hon. Hampton L. Carson

"THE COLLEGE AND ITS TRADITIONS"

Dr. Arthur V. Meigs

DINNER OF THE COLLEGE OF PHYSICIANS OF PHILADELPHIA ON THE OCCASION OF THE DEDICATION OF ITS NEW HALL.

November 10, 1909. The Bellevue–Stratford.

Dr. James Tyson:

In one of those quaintly worded speeches characteristic of his day, Dr. John Redman, the first President of this College, congratulated himself on the "aid and support" he expected to receive in his office from the then newly elected Vice-President, Dr. William Shippen, Jr., thereby rendering his "situation the more easy and pleasant while he remained in it." I, too, am favored in having for Vice-President one whose fondest wish is to aid and support me by such assistance as will lighten the burdens which fall to me in the execution of my office, thereby rendering my "situation the more easy and pleasant," while I remain in it. Moreover, so gracefully is this service rendered that he is much admired of men in consequence. None of these offices does he so well adorn as that of the master of the ceremonies, which he has kindly consented to assume tonight. I have great pleasure in introducing Dr. George E. de Schweinitz, the Vice-President of the College and toastmaster of the evening.

The Toastmaster:

There is one who fifty odd years ago entered the ranks of our Fellowship, and the College grew strong and stronger; he turned the light of the lamp of his genius on dark places in the field of medicine and they became clear and clearer; he approached

unsolved problems in physiologic science, neurologic practice and therapeutic studies, and their meaning became plain and plainer.

A keen observer, a constant investigator, a wise physician, his results have sweetened the lives of those once bitter with the sorrow of mental and of physical ills. A generous friend, he has freely bestowed the gifts of his inspirations and the stimulus of his suggestions, making success possible for him who has asked and received his help.

He has "grazed the common of literature" and the hours of those who read are brightened; he has "tuned his harp, and, like a river swift and clear, flows his song through many a heart." Physiologist, physician, author, and poet.

> "Hail thou! akin to that immortal band
> Whom age has touched not with her finger frore;
> Take thou thy lute within thy charmed hand,
> And smite the strings once more."

For "The Old College and the New," S. Weir Mitchell.

Dr. S. Weir Mitchell:

Mr. President and Fellows: My only regret tonight is that we are unable to dine in the Memorial Hall of our new College. The number of our guests forbids it. Indeed, had we dined there, we should have missed the pleasant audience of the gallery. They, in truth, I sometimes think, have the best of it. They have no after-dinner speech on the festive horizon, nor are they troubled with that form of mental indigestion which reminds a man after he has made his speech of the clever things he might have said and did not. It is what the French aptly call *esprit de l'escalier*.

But this is not for me an occasion for the gay nonsense of the after-dinner hour. Indeed, for more than me the ceremonies of these two days have a certain solemnity from which it is scarcely possible to escape. There is an echo of this feeling in the toast assigned to me: "The Old Home and the New Home;" the old College and the new. My toast might be put in other words: "Our Memories and Our Hopes."

My own memories, indeed, are somewhat ancient. The first meeting of the College I attended after my election, in 1856, was in the little "picture house," as it was called, of the Pennsylvania Hospital, on Spruce Street. There is not here tonight a single Fellow who was present with me on that occasion.

The men to whom I then looked up are dead. As dead as they, are the theories they fiercely debated. Of the drugs they employed we use but few. Could these physicians return for a ghostly consultation, the practice of medicine to-day would be to them an amazing revelation. In fact, we are the most revolutionary of the professions. We try, condemn, decapitate the thought king of today and crown a wiser king of tomorrow, forever changing and forever changing for the better.

There may be some here who share with me my first remembrances of the home we are leaving at Thirteenth and Locust Streets. We built it with difficulty, amid the civic unrest and thunder of war in the year 1862–63. Alas! too many whom I then knew, my friends, my comrades, my rivals of those earlier days, have carried the memories of our former home to that better home where, surely, all physicians go.

In those halls, in the days when the sciences were so rapidly changing, we broke the lances of debate, announced our discoveries in medicine, and did, I think, our ample share in contributing to

> "That noblest art
> Which asks alike head, hand, and heart."

That, too, was our social exchange for the pleasant greetings of busy men. There the young were helped with counsel; there friendships were made; there, on the common ground of work, the rivalries of schools were set aside under the eyes of our medical ancestors, whose grave portraits looked down upon us from the walls.

For me and for many of you our great library is generous of pleasant remembrances. What helpful, fertile study it has known; what noble friendships with the great books; what happy assurances that in some new discovery we had not been anticipated.

Those crowded shelves hold for the imaginative the inspiration and thought of two thousand years of our ancient guild. They remind us that, long before Christ was born, we had in the creed of Hippocrates the noblest code of honor then known to man. A great library like this offers food for the mind, and even matter for the moralist, since in the biographies of our greatest are to be read lessons in the patience and humility of genius, and in the rectitude of lives morally and mentally exemplars far above what is represented in the lives of the historic soldier or the great lawyer. Nor did we lack material reminders of services rendered, of duty done. In our old hall a tablet recorded the names of those who fell on the battlefield or in the wars with pestilences.

In our new hall a like roll of honor will commemorate a sense of duty as great as that of our founders, so many of whom shared with the great Virginian his long years of anxious trial. On this other tablet we shall place the names of 160 Fellows, who served the country on land or sea as surgeons during our great Civil War.

With many of you, I shall miss the familiar surroundings which belonged to our old hall—a home both of the heart and of the mind. As I speak, the portraits of our presiding officers and distinguished Fellows come before me. It is a long and noble line, these Presidents, beginning with John Redman, in 1787. There too, were those of a later day—the men we have known. From our walls looked down on us the serene face of George B. Wood, the first of our large benefactors. There, too, was the gentle gravity of the accomplished Stillé; the strong, sweet face of the much loved Agnew; Da Costa, courteous, learned, and trusted; Ashhurst, the surgeon; the manly beauty of the elder Gross, and the face of James Hutchinson, dear to many and most dear to me. Some survivors of the Presidency still exist. One of them is sadly missed tonight, and wherever eloquence and science are valued; need I name our former President, Horatio Wood?

I like to think of these silent onlookers at our debates, not only as masters of medicine, but beloved as was the physician beloved of Christ.

Let us carry from this our old home the splendid challenge of the past into that home of the future, that new College which is, as you will see tomorrow, the most stately edifice which the greatest of professions has anywhere built. It is at once a home, a monument, and a temple of medicine. We have brought thither our household gods, our relics, our portraits. We shall people it with new memories and not forget the old. What it will hear in the next century I vainly guess. It will surely have heard of the end of diseases which we think of now with anticipative terror. Before that century has gone, tuberculosis will have been conquered, cancer will no more demand the services of the surgeon. Prophetic dreams of today will become the fulfilled realities of our many tomorrows.

The follies and intrusions upon our own ground of the quack and empiric, of the inventor of new medical religions, have been in the past and will be in the future, nor are they always without their suggestions of value. In all ages we have had to deal with the quackery of opinion, and we have it still in the anti-this and anti-that—a large family—the hysteria of anti-vivisection and the inconceivable folly of anti-vaccination.

Armed with the inspiring thought of what we have done for mankind, of that archangelic work which has put an end to pain, has conquered malaria, yellow fever, and smallpox, let us go tranquilly on our useful way, and in our new home take up once more our dutiful labor.

I close, with satisfied pride, these brief annals of the past and its day. I see about me men whose books are in every tongue of Europe, whose works are known among the learned of every land, men who wear by just decree the unseen crowns of honorable estimate. I see, too, before me the young of my profession. To them we shall soon consign this precious heritage. There is in the long years of this College that which should make them proud of a Fellowship which, in war and in peace, has left us examples of single-minded duty; of charity without taint of selfishness; of lives lost in battle with disease; of daring surgeons, whose very

fingers seemed to think; of physicians rich with every professional and social grace.

Pride of lineage is valueless if it does not insure for the future fertility of usefulness. I must have told my story ill if what I have said does not have for some of you the invigorating force of a moral tonic.

I turn from the past to a cheery present, and face with the comfort of certainty the silence of the eager years to come. I should be other than I am if I did not linger a moment to translate into speech the language of the heart, and to say what I cannot easily say, how gratefully I thank this Collegiate Fellowship for a too flattering material expression of the affection which has meant so much to me through these many years of a laborious life.

THE TOASTMASTER:

Fellows of the College, fortunate are we in the presence here tonight of our guests, who by their worth thus dignify our feast, and turn we now to one who

". . . is happily arrived,
My mind presumes, for his own good and ours."

For ours, that we may here proclaim aloud our grateful, happy thanks for that most generous gift whereby is built a home—ah! how beautiful a home—wherein our venerable library now is fitly lodged; for his, that he may know, as it is but right that he should know, how far-reaching will be the impetus of that which he has done upon

". . . the art whose glory is to give,
The crowning boon that makes it life to live."

A world-renowned lover of books, and a master of the art of giving, his munificence has made easy the access of all book-lovers to the "gathered thoughts of men;" a student of governmental problems, he has placed sign posts for the onward march of a triumphant democracy; a hater of the horrors of war, he has housed the arbiters of the nations and nourished the brotherhood of the

peoples of the earth; a friend of education, he has established a mighty foundation on which the students of the world find means and place to add their quota to that temple of knowledge which grows fairer day by day. A great alchemist, the iron in his crucible turned to steel, the steel to gold, and the gold to opportunity; opportunity to aid the oppressed, to halt a stalking pestilence, to reward the brave, and to open gates to knowledge throughout the world. "Libraries and Their Foundations," Andrew Carnegie.

MR. ANDREW CARNEGIE:

MR. CHAIRMAN, AND YOU, PRESIDING OFFICER: After listening to what our friend said, it seems to me such a descent to speak upon any ordinary subject. I would that we could have had not one word said after that address, and that we should go home with it thinking that in that half-hour's speech we had everything that would enable us to go home saying, "The most perfect ceremony I have ever attended!" (Applause.)

But, Mr. Chairman, it is ordered otherwise. Behold the victim of misplaced confidence! (Laughter.) I thought the speech-making came at the banquet to-morrow night; and, as I had engagements and had to leave to-morrow morning, I didn't have the slightest idea that I was to be called upon to address you. And then the subject—"Libraries."

"O, what a fall was there, my countrymen!"

But I find that great lights in a profession, illuminated with all the brilliant lights around them, are very apt to be just not quite as well informed upon other subjects as they might be. No man can know everything of all the professions; and your talented Chairman tonight asked me whether I was satisfied that the more than two thousand libraries I had given (and, I believe, about fifty-five millions of dollars devoted to libraries)—whether I was satisfied that they would yield a satisfactory return.

Now, I was glad he asked me that, because that gives me some excuse for answering the question. I say, that if I had to choose

again what branch of usefulness I would embrace, the first thing I would do would be again to say to every community of the English-speaking race in any part of the world: "Any community that will furnish a site and maintain a free library, I devote this money to, as the best use that I can make of surplus wealth." (Applause.)

Ask your admirable Librarian here (because, whether a library is worth living or not depends upon the librarian) — ask him what he can tell you about Philadelphia. He will tell you that he circulated two millions of books last year, and that four millions of books were read in this city by visitors to the various libraries.

It is not what a library does that ends the account. It is quite as much what it prevents. Where would the young men be if they were not in the library? And the hundreds of letters that I have got from parents (I keep them now in a box), especially from mothers, telling me that the opening of the Free Library in their town had changed their boy; that he was there every night, and he was pursuing the subjects which appealed most to him! Now let me tell you what Mr. Thomson told the Chairman just now: A boy pursuing any profession, going to pursue a profession—an apprentice—can go into your library this year and he can get from the librarian the list of books bearing upon the very pursuit that he is engaged in. He is carried along. We find in Pittsburgh, in our technical schools, where we have already 2000 boys —we find the libraries near them the greatest benefit. They study in the technical school and they go to the library for the very authorities that are needed.

There is another point wherein the library goes to my heart. It doesn't do one thing for anybody for nothing. (Applause.) A young man has to help himself before the library will help him. (Applause.) That is another great point about a library. You get nothing for nothing, and the bright boys are those that get all the advantages from the library.

I have done rather a wholesale business in libraries (laughter), and two gentlemen in this room are responsible for getting more than 100 libraries. You and Mr. Thomson—well, Philadelphia

why, what oughtn't I do for Philadelphia? It was my second home when I was a young man. In Pittsburgh I was called here often by my superiors, that they would give me instructions; and sometimes I think I gave them a few instructions. (Laughter.

I was great for quoting Shakespeare and other poets; and, do you know, I got a great reputation among my colleagues? More than once the quotation was taken as original. (Laughter and applause.) I certainly traded on borrowed capital to a great extent in my youth.

Now, Mr. Thomson got thirty libraries—Philadelphia. I was very often here, as I told you, and I had a second home in the home of my dear friends, Mr. and Mrs. Franciscus, 1823 Chestnut; a room was there for me, kept for me, to be taken advantage of at any time; so that I claim kindred with you people of Philadelphia, and I gave those thirty libraries with intense satisfaction. But this gentleman, Mr. Billings—well, the gallery may not have heard as much of him; he doesn't play to the gallery so much as to these learned gentlemen below; he called one morning, and he walked out of my house with a little document giving him seventy-eight branch libraries (applause)—the greatest wholesale order (and yours the second) that I have ever had the advantage of filling. Throughout the days afterward occurred congratulations: "Hello! I congratulate you, Mr. Carnegie; I congratulate you." "Hold on!" I say; "what for?" "Why, for giving New York seventy-eight branch libraries." "Can't accept your congratulations. But if you will congratulate me upon having induced New York to sustain seventy-eight libraries, open to all the people, shake!" (Applause.)

Now, I rate the money I give as of very trifling moment, comparatively. And I say the money that a community itself gives to open a collection of books, the people's university, to all the people—I say that is the action that counts, that is where money tells; and what I give may only be considered as the fly with which we catch the fish. So much for libraries.

But, Mr. Chairman, I may say that I come by library building by inheritance. My father was a poor weaver in Dunfermline;

and there stand the records that he was one of five that bunched his books and opened them on a little stand in his room—shop—for all the people to read; and that library was moved seven times, from one place to another, always to grander quarters. He furnished the first library for Dunfermline, and his son had the privilege of establishing the present library. I have never known a lineage for which I would exchange that of a library-founding weaver. (Applause.) So much for libraries.

Now, one word more and I am done. I hope I have answered your question?

MR. ——: You have, really!

MR. CARNEGIE: Now, this is a doctors' meeting; this is the medical profession, and we have heard how it has progressed; and no profession has obtained greater victory over ignorance than the medical profession—none whatever. What you have recounted there, that is history; but there is much to be desired yet from the medical profession. I hear so many different views given as to the right mood—of doing this way, that, and the other, and what is best. It reminds me of my friend Josh Billings in his almanac. You know he printed a paper once a week, and a feature was, "Answers to Correspondents;" and one correspondent writes:

"My Dear Editor: I see in all the papers that they have discovered that fish—fish is the best diet for producing brain power, because of the phosphorus; but there isn't any editor that is wise enough to tell us what kind of fish is best"—and that is the trouble with your profession. Well, Josh Billings answered:

"In your case, try a whale or two." (Laughter and applause.)

Now, the gentlemen of the medical profession must—and of course they will—they must, because they follow science and the star-eyed goddess of Truth, they will eventually come to some settled conclusions; so that we men, anxious to have long life and good health, and everything of that kind, will know just exactly what kind of fish it is that we should each take.

Gentlemen, I came to Philadelphia tonight at the call of one whom it is a delight and an honor to obey. When I settled upon

the research commission which is now, I am delighted to say, attracting the attention of the whole world for its work, I wished all the parts of the country to be represented; and there was one man in Pennsylvania, right here in Philadelphia, that I had heard enough about and had read about—and then I inquired from various people, and I said: "I will address Weir Mitchell and ask him to represent this section of the country." (Applause.) Of course, he responded. From the acquaintanceship then formed it has ripened into friendship, and it has passed the friendship stage and ripened into admiration, and it has passed that stage of admiration, and I say, now, I have reached the stage of genuine love and affection for that man. (Applause.)

I believe this to be the apotheosis of his career. I cannot believe that anything can be produced in Philadelphia—and, of course, it won't count if it is produced anywhere else; nothing, no triumph, no ceremony, no honor can be bestowed upon him that can quite equal this night, at the very apex of his life; and I account myself happy that I am here present tonight, that I look upon this scene, and that I know that as long as memory holds its seat in my brain, in my happier moments I will revert to this great night, where I met you all, and where I sat next Weir Mitchell; and as I speak the word, it doesn't—it doesn't lessen my affection and my love for him to know that there is a wee drap blood atween us. (Applause.) We trace our heritage to Scotland!

> "And may dishonor blot my fame,
> And quench our household fires,
> If me or mine forget thy name—
> Thou dear land of our sires!"

He is not a more triumphant-democracy American than I am. That man don't live. Every day that I return here, every time I think of it, Ah, I think of the glorious democracy! Six lines from Burns, I heard John Morley say, held the doors of the empire; six lines of Burns affected the political thought and progress of the world more than all the editorials that have ever been written; and what were those lines? He said to me, "I need

not ask you if you know." I said, "No; I know two of them." What? Burns—his call to the Republic when she was struggling:

> "Columbia's offspring, brave and free,
> Still flaming fire in danger's band,
> Ye know, and dare proclaim
> The royalty of man"—

and these are two of the lines from Burns.

Weir Mitchell showed me a book with Burns' name in it tonight. He gets his lessons, too, from that great Democrat. He was a good American before America was; and we are good Americans now in our lifetime, and we will die good Americans. (Applause.)

One word and I am done. Here he stood today, here he sits; and all that can accompany old age he has—honor, love, obedience, troops of friends, and all these you have, my friend, and the record you leave behind you, of which none of your survivors will feel ashamed. (Applause.)

THE TOASTMASTER:

In the notable company famous in the surgical achievements of the city there is one conspicuous in his success, untiring in his devotion to the exactions of professional duty, marvellous in his unflagging industry. An anatomist, he has demonstrated that surgical dexterity must be the outcome of intimate anatomical knowledge; a surgeon, he has accepted bravely his great responsibilities and performed his duties with consummate skill; an author, he has enriched the literature of his art and has inspired those who came within the range of his instruction to add to their quota the records of our craft; a teacher, he counts his students by the thousands, who have carried throughout this land to those who surround them the wisdom of his advice, the worth of his lessons, and the value of his uplifting influence; a citizen, he is true to the duties of citizenship and valiant in the battles for civic righteousness; a lover of books, the precious burdens on the shelves of our Library have

grown greater because of his unfailing interest and generous help. "The Library and its Treasures," W. W. Keen.

Dr. W. W. Keen:

A distinguished savant on one occasion was reproached by a lady friend for having almost no library. The story runs that he replied, "Madam, whenever I wish a book on any subject I write one." Few of us are so versatile, so audacious, and so witty. We have to rely for our books largely upon others; hence the library.

We have now installed in our new building the largest, most important, and best-housed medical library in the United States, except that splendid boast of America, and indeed of the world, the Surgeon-General's Library in Washington. The dedication of this building, the counterpart of which does not exist on either side of the Atlantic, marks an epoch for medical libraries and for medical societies in the United States. It has every modern improvement, including, of course, a highly ornamental and highly interesting debt.

The foundations of the Library were laid in 1788, when the College was only one year old. Excluding duplicates, it now numbers 81,018 bound volumes—you see I am very exact—besides 8202 unbound volumes. In addition, we have 93,924 unbound theses and other pamphlets. Were these all bound—a task we are accomplishing as fast as our limited funds will allow—the number of volumes in our Library would equal, or more likely exceed, 100,000.

The Library is open to all who wish to use it, not only men and women of all schools of medicine, even including the medical guerillas, but to any and every person who has a need it can supply.

In our new building, as you have seen, it lures the reader by its comfort and its unsurpassed facilities. Once in its silken toils it is hard, nay, often impossible, to tear one's self away.

One feature I think is unique, and will double its usefulness. We have twelve small private study rooms, where any Fellow engaged in a prolonged and serious research can shut himself off

from interruption, and, surrounded by his books, can make his notes or dictate papers; and, when called away, simply turn the key and find everything undisturbed when he returns. The saving of time to the student and to the Library staff, and the saving of wear and tear to the books are great, but by no means the greatest advantages. When everything invites to research, and it is made comfortable and relatively easy, even the half-hearted may be enticed or goaded to such work. My only fear is that we shall not have rooms enough, for it is a credit to our Fellowship — and I mention it with pride — that for years past 10 per cent. of our Fellows every year have either published new books or new editions, while the number of journal articles written by them would make a surprising total.

We grow by purchase, gifts, and bequests, and as I look around me I see generous donors, whose names are enshrined upon our shelves on the book plates in many a handsome octavo, solid quarto, or sumptuous folio. It has long been a well-established rule for every Fellow to bequeath his library to the College, unless there is a lineal descendant who may need it, and anyone omitting such a provision in his will is believed seriously to imperil his future salvation.

Of the two large reading rooms you have admired, one is for the perusal of books, where many hundreds of reference books are always accessible, and in the other there are the most important of the 950 medical journals and other similar serial publications we receive. Our present stack, provided with every device for safety and every means for quick and satisfactory service, will accommodate 300,000 volumes, with the possibility of almost indefinite future expansion. All our books are stored there, with two exceptions — the reference books already alluded to, and the Gross Memorial Library, a cherished memento of my own revered teacher and predecessor, to which has been allotted a special room.

Moreover, we exchange with twenty-eight foreign universities. Our files of theses and dissertations, therefore, are unusually complete. Our set of the Paris *Theses* from 1798 to 1882 is as yet

imperfect, but from 1882 to the present it is complete, and we now obtain each annual issue of forty to fifty volumes as they appear.

Truly, we have provided materials for widespread intellectual indigestion.

But I must not linger over the installation of the Library, but say a few words about the books themselves. Here you will find a most diversified company—from the Greek Diascorides and the Latin Celsus to the English Lister, the American Gross, and the cosmopolitan Osler; here French Louis and German Langenbeck greet each other most cordially; here Russian, Finn, Pole, Swede, Japanese, Italian, Spaniard, and the dwellers in Roumania and Mesopotamia—all peoples and tongues—can do more than speak to us; they can keep silent in all languages, yet to him whose eye hath been annointed their illuminating pages are full of inspiration.

Here, in the Library, you will find the *πον στω* of Archimedes and the levers which have really moved the intellectual world. And how tiny some of them are! Darwin's *Origin of Species*, only as large as an ordinary novel, shook the whole world of thought; and that little pamphlet (for one may so call it) of only fifty-two pages of text, Harvey's *De Motu Cordis et Sanguinis*, overthrew medical systems hoary with the authority of centuries, and ushered in a new era. Other books belong to the "literature of knowledge;" these to the "literature of power."

We have most of the classics of medicine, for our older Fellows were good Grecians and Romans. Of the very earliest books, we have 148 printed in the fifteenth century, from 1470 to 1500, an extraordinarily large collection of the incunabula of medicine. Some of them are among the rarest of the rare. One is a copy of the first medical book ever printed (1470); others are the first medical dictionary and the first books on diet, on diseases of children, and diseases of the eye; while our de Kethams, Avicennas, Ambroise Parés, Morgagnis, Vesaliuses, and Harveys are not only valuable in themselves, but, in the words of Osler, they "give tone to the shelves, just as do the Stuarts and Copleys to the dining room of an old mansion." *Editiones principes* of Auenbrugger,

Laennec, and Jenner, the last with his autograph and inscription, are among our boasted treasures.

Of Americana, we have the first American medical journal, Cadwallader's treatise on the *West India Dry Gripes*, printed by Franklin in 1745, the only known copy containing the two prefaces, one of which was afterward suppressed; John Morgan, *On the Medical Schools in America*, printed by Bradford, in 1765; a copy of the first Medical Practice Act in the United States, also printed by Bradford in 1794, and many other literary *bonnes bouches*, which make the bibliophile's mouth water.

Of the 3082 medical portraits—all card catalogued, and many more as yet uncatalogued—the medals, book-plates, diplomas, lecture tickets, and medical curios, I have no time to speak, save to mention, among the last, a lock of Jenner's hair, a stethoscope of Laennec, a set of Perkins' tractors, the knocker from the door of Ephraim McDowell, and a real bookworm.

Is it any wonder, then, that even in our old cramped quarters we have had over 12,000 readers in a year, and that we expect the number quickly to double in the new home provided for us, chiefly through your generosity?

Such a Library is of far wider service than to the profession alone. It cultivates the habit of reading and of study in the whole community; it breeds better doctors for the City, the State, and the Nation; it renders research a pleasure as well as a duty; it aids in keeping America abreast of Europe, and helps to keep Philadelphia the medical centre it has always been. As such, it justly appeals to our citizens for support, and especially for endowments, which may well take the form of pious memorials of the cherished dead.

What now can I say to you younger Fellows of the College? We, your elders, and before us the fathers, have labored for a century and a quarter, and ye have entered into our labors. I am sure that you will use this splendid Library diligently, will add to its value, will adorn its shelves with many a noble book whose title page will bear your own names, rapidly growing famous; and in gratitude you will always bear its needs in mind and give it freely

of your substance. Here will Weir Mitchell's stimulating spirit and his counterfeit presentment look lovingly on the growing treasures he has done so much to gather and to house, smiling a benediction upon countless future readers, his grateful debtors, long after he has passed into the happy land where neurasthenia is not known and the rest cure of "Ver Micelli" is not needed.

THE TOASTMASTER:

Turn we now to one who may trace his relationship to one of our founders, to the son of a distinguished member of the College, and to a friend, and the representative of a very generous friend, of all of us gathered here on this notable occasion.

A scholar who has exposed the fascinations of our Colonial history and enriched the collections of our historic art; a lawyer renowned in his profession, bearing with honor an honored name, and striving for the principles and practice of legal rectitude; an advocate pleading the cause of justice; a servant of the public, maintaining with dignity and distinction the difficult and arduous post of the first legal officer of this great Commonwealth; a teacher successfully training those who would join the profession which he so well adorns; an orator stirring his audience with the lucidity of his revealing eloquence. Hampton L. Carson: "The College and its Civic Relations."

HON. HAMPTON L. CARSON:

MR. TOASTMASTER AND GENTLEMEN: In rising to respond to the toast which has just been offered, I appear in a representative rather than a personal capacity, and hence I speak for others as well as for myself. On this auspicious occasion I bring you good wishes for the continued strength and usefulness of the College of Physicians, from the noble-hearted and generous woman—Anne W. Penfield, wife of Frederic Courtland Penfield, and daughter of the late William Weightman—whose name will be held in everlasting gratitude as a munificent contributor to your building fund. I bring you also the felicitations of your sister profes-

sion of the law; I bring also an inherited pride and interest in your welfare, endeared to me by tender associations; so that I am happy in this opportunity of expressing sentiments which command a willing spirit and a grateful heart—a spirit willing to rehearse your good deeds, a heart grateful for the benefits you have bestowed upon your fellow-men. Well may it be said of your institution that you have fulfilled to the letter, as well as in spirit, your motto, *Non sibi sed toti*. Judging your future by your past, and regarding with steady eye your honorable present, I may add the words of Tacitus in describing the well-spent life of Agricola: *vivit, vivetque ad sempiternam ætatem*.

I had the privilege last Saturday afternoon of visiting the New Hall, under the guidance of one who, whether he be regarded as physician, author, novelist, poet, or cicerone, as interpreter of the past, as guardian of the present, or herald of the future, is always in the lead. As I scanned the names of your Presidents and Vice-Presidents, your Censors and Secretaries, your Treasurers, Librarians, and Councillors, and the long roll of distinguished members; as I gazed at your pictured walls and saw the strong and expressive lineaments of Redman, Shippen, Morgan, Kuhn, Parrish, Meigs, Wood, Ruschenberger, Pepper, Da Costa, Hutchinson, Gross, and Leidy, the dead became alive again. As I look into the faces of the men now before me, and see those renowned in medicine and surgery—as I look up and down this glittering line—the living become assured of immortality as I discern the features of Mitchell and Keen. I see a "goodly fellowship," and "noble army" of saints, martyrs, and soldiers in the cause of humanity, whose knowledge, skill, industry, fortitude, and patience are devoted to the relief of suffering, the expansion of science, and the elevation of society, by checking the ravages of disease. In truth, since Colonial days, and the periods of the Revolution, and the Framing of the Constitution, down through the War of 1812, the Mexican War, the Civil War, and the war with Spain, and the long intervals of peace between, your relations to the City, the State, and the Nation have been close and influential, mitigating the evils of the one and emphasizing the blessings of the other. Your members

have been the intimates of those who shaped our counsels, fought our battles, and moulded our decrees. It was Thomas Bond and Thomas Cadwalader who were associated with Franklin in founding the Pennsylvania Hospital; it was Morgan, Shippen, and Rush who trod with Washington the bleeding snows at Valley Forge; it was Hewson who faced the raging of the yellow fever in 1820, as it was Chapman who was the hero of the cholera epidemic in 1832; it was Physick who saved by his knife the life of Chief Justice Marshall, the greatest constitutional jurist that America has ever seen; it was Wistar who was the confidential friend of Chief Justice Tilghman; it was Woodhouse who served with the army of St. Clair, just as it was Brinton who served with the army of Grant; it was Pancoast and Gross who walked the hospitals in the midst of civil strife, as it was men of today who braved the dangers of the camps at Chickamauga, Porto Rico, and the distant Philippines. It is men of your profession who have suggested many of the most beneficent of our statutes, guarding the portals of the profession against the intrusion of the charlatan and the ignorant, protecting the children of our public and private schools from smallpox, establishing the jurisdiction of our Health Department, securing the purity of our water supply, controlling the system of sewers and drainage throughout the entire State, teaching the ignorant the rules of sanitation, and educating the wealthy in the noblest forms of altruism. It is you who "do good by stealth, and blush to find it fame," and clasp hands with the great philanthropist in giving mountain air to the victims of the White Plague.

Consider the relations of the College of Physicians with the University of Pennsylvania, the Jefferson Medical College, the Medico-Chirurgical, the Pennsylvania Hospital, the Episcopal Hospital, the Presbyterian, the Methodist, the Polyclinic, St. Vincent's, and all our constellated jewels of charity, the Philadelphia Hospital, the American Philosophical Society, the Academy of Natural Sciences, the Franklin Institute, and the Philadelphia Library. Strike all these out of existence, or blot out the recollection of the lives and labors of your foremost men, and what an intellectual, moral, scientific, hygienic, and social bankruptcy would ensue.

When Lord Bacon devised the fable of the New Atlantis, to the end that he might exhibit a model of a college instituted for the interpretation of Nature, and the production of great and marvellous works for the benefit of men, he fitted it into the framework of an ideal commonwealth, and commended it with the blessing of God to the "good of nations." He laid particular stress upon the prolongation of life, the restoration of youth, the retardation of age, the curing of diseases counted incurable, the mitigation of pain, the increasing and exalting of the intellectual parts, the force of the imagination, either upon another body or upon the body itself, the drawing of new foods out of substances not yet then in use. He wrote of "some degrees of flying in the air," of ships and boats for going "under water," and of means to convey sounds in trunks and pipes in strange lines and distances. The vastness of his mind — and, let me proudly add, it was the mind of a trained lawyer as well as a philosopher — was illustrated in thus prefiguring inventions and discoveries which translate themselves today into medical, surgical, scientific, electrical, submarine, and aeronautic terms, and placing them in association with the State. It was but an anticipation of much that you have done in the establishment of your civic relations through the practice of a learned profession.

In the same spirit of prophecy, let it be predicted that your descendants, contending with death, disease, and filth, will see the day — God speed the hour — when swords and bullets, sashes and epaulets, shall vanish with the fevers of the camp and the ragged wounds of war, because the nations, in the fulness of time, will exchange violence for the true meaning of the mission of Him who came to proclaim peace on earth and good-will toward man.

THE TOASTMASTER:

There is one who has upheld and advanced the prestige of a distinguished medical ancestry in the fields of clinical research and of clinical practice; who has entered the province of histologic investigation, pursued his studies along original lines, and recorded them with scholarly precision; who has served the College, and

that right loyally, as friend, councillor, and President, setting and steering straight her course with courage born of conviction, following ever the call of official duty and maintaining it with quiet dignity. Earnest in purpose, constant in effort, efficient in practice, that to which we cling so proudly and which he so well and bravely exemplifies, becomes his toast — "The College and its Traditions," Arthur V. Meigs.

Dr. Arthur V. Meigs:

The College and its Traditions! It would take much time to do full justice to the theme that has been assigned me, for the College is an inexhaustible subject to all of us; and, as tradition includes not only that which has been handed down by word of mouth of opinions, customs, and practices, but also that which is embodied in literature, the subject covers the whole history of the institution. Do not, however, be alarmed, for I shall not attempt to give you a complete history.

It requires but little consideration of our traditions to make it plain that from its institution the College has been able to command the interest and best efforts of the wisest and strongest men in the profession of medicine in Philadelphia. The founders, and, since their time, the foremost men of every generation of physicians of the city, have given unstintingly of their time and labor to the College. Why have the leading men of the profession since 1787 been willing so to labor for a society that was able to give but little in return? The men of the pas and we of today—I firmly believe —are attracted and bound to the College because its tradition is that the society must always make the elevation of the profession of medicine its principal end. Do not, I pray you, listen to those who preach pessimism, and tell you that physicians have become mercenary and that the profession has departed from the altruistic standards that our forefathers in medicine upheld. It is not the possession of a superb library and a handsome hall that has given this medical society its preëminent position. These are adjuncts that are almost necessary, and a noble hall, such as we have just dedicated, is no more than a fitting setting to the work. It is not,

however, these things that give to the College its position, but its noble traditions, which had their foundations laid at the beginning of the institution, and which we of today must firmly hold, and hand down unbroken to our successors.

Let me tell you what I believe is one source of the strength of the College—it is its freedom from entangling alliances. Our society stands entirely alone at a time when combination is the common order of the day. The College has heretofore been so prosperous, and has increased so rapidly in size and power of usefulness, under the policy of standing aloof, that for my own part I should be sorry to see it enter into a formal combination with any other organization. Perhaps you do not all know that the College was one of the societies that founded the American Medical Association, and for a number of years we regularly sent delegates to that body, which has now become so large and powerful and useful. After a time it was decided that only State and county societies could form parts of the Association, and the College was deprived of its membership and rights, to the great indignation of some of our Fellows, as I have myself heard them say. There must have been a good deal of bitterness of feeling at the time. Now, however, it seems to me quite evident that the separation has been of advantage to both organizations. The College, I think, must have been swallowed up in the larger body if the relation had been continued, and to have continued it, could have added but little strength to the American Medical Association, which was quite able to stand alone. Although we have no official relation with any other organization, we have for a good many years lived in the same building with most of the medical societies of our city, and our mutual feelings are those of respect and good wishes. I am sure that I truly represent every Fellow of the College of Physicians when I say that we ardently hope for the prosperity of every one of the good societies that shares with us the shelter of a single roof.

A glance at Dr. Ruschenberger's book, *An Account of the Institution and Progress of the College of Physicians of Philadelphia during a Hundred Years*, reveals much that is interesting and at the same time shows that we of today should be encouraged.

It is evident that our forefathers had some triumphs, and that their difficulties were very like our own, if reasonable account be taken of the difference in the size of the organization, and that everything with which we deal is, therefore, upon a larger scale. For instance, it is recorded that "the Treasurer reported, June 3 (1862), that $5000, loaned on the security of a mortgage, had been deposited in bank to the credit of the College. The payment of interest on that loan continued to be a serious encumbrance, and there was no prospect at any time that the society would ever be able to pay the principal." In comparison with the sums with which we deal today, imagine a debt of $5000 being a "serious incumbrance." The city of Philadelphia has indeed grown since 1862, and the College with it. Although we are sometimes in ill humor for a time after municipal elections, upon the whole we may well be proud of the growth and prosperity both of our city and of our College.

It always seems to me that the preservation of the records is one of the most important things for any combination of men forming a society if they expect it to endure. The records of the College are dignified, and they tell its history. It is easy to see that many difficulties were overcome in the past, and by reading between the lines it can be recognized that grave differences of opinion arose, which might indicate that there were quarrels. Time has smoothed out the rough places, and we have reason to be thankful that the records were kept by faithful secretaries, who wrote in measured phrases, which told the history of action and ignored the petty things.

No after-dinner speech, I suppose, could be considered complete without a story, and, therefore, I shall tell you a short one. When I was a boy, I was sitting one day with the late Dr. Charles D. Meigs, who was for a good many years Vice-President of the College, and by some chance I asked him about his bills and professional charges. His answer was brief. "By George," he said, "no man ever paid me for my professional services; the world is so organized that I am obliged to accept an honorarium." Through a long and arduous life as a physician in practice, and as a professor in a college, he had followed that principle, and at

the end, after he had retired from active work, he believed in it more firmly than he had at the beginning. You are asking yourselves, perhaps, why does he tell us such an Old World and foolish story? Gentlemen, my story is neither Old World nor foolish; it is not even impractical; for the principle involved had been the sheet-anchor during life of a man who started without influence and rose to the best kind of success. At the end of his life he was supported in a philosophical and dignified old age by the remembrance that that principle had guided his daily actions. Why *have* I told my story? I have told it in order to show you the sort of men the College formerly contained, and to give *me* an opening to declare my belief that the roll includes today the names of as good men, and men as altruistic, as have been in it at any time since its foundation. *These* men will carry on its traditions, which is to discourage all that is evil, and to strive continually for the elevation of the profession of medicine.

LIST OF GUESTS ARRANGED ALPHABETICALLY.

Abbott, Dr. A. C.
Adami, Dr. J. G.
Adler, Dr. Louis H., Jr.
Allen, Dr. F. O.
Allen, Dr. Dudley P.
Allen, Dr. Alfred R.
Allyn, Dr. H. B.
Anders, Dr. James M.
Andrews, E. W.
Anspach, Dr. B. M.
Appel, Dr. Theodore
Ashby, Dr. Hugh T.
Ashhurst, Dr. A. P. C.

Babbitt, Dr. J. A.
Baer, Mr. Geo. F.
Baker, Dr. George F.
Barnard, Dr. E. P.
Baugh, Mr. Daniel S.
Baum, Dr. Charles
Beardsley, Dr. E. J. G.
Beates, Jr., Dr. Henry
Beaver, Hon. J. A.
Bent, Major Luther S.
Beyea, Dr. H. D.
Billings, Dr. J. S.
Billings, Dr. Frank
Blakiston, Mr. K. M.
Bland, Dr. P. B.
Blumer, Dr. G. A.
Bochroch, Dr. M. H.
Bodine, Mr. Samuel T.
Boyd, Dr. G. M.
Bradford, Dr. T. Hewson
Bradley, Dr. William M.
Branson, Dr. Thomas F.
Brinton, Dr. Ward
Brown, Mr. Stewardson
Browning, Dr. W.
Brubaker, Dr. A. P.
Bryant, Dr. Jos. D.
Bull, Dr. Chas. S.
Burr, Dr. Charles W.
Butler, Dr. Ralph

Cadwalader, Dr. Williams B.
Cameron, Dr. George A.,
Carmany, Dr. H. S.
Carnegie, Mr. Andrew
Carrow, Dr. Fleming
Carson, Mr. Hampton L.
Cattell, Dr. H. W.
Cattell, Dr. J. McKean
Chance, Dr. Burton
Chapin, Dr. John B.
Chase, Theo. L.
Chase, Dr. R. L.
Chatard, J. A.
Cheston, Dr. D. M.
Cheston, Dr. Radcliffe
Christian, Dr. H. M.
Christian, Dr. Henry A.
Clark, Dr. John G.
Clarkson, Dr. J. A. C.
Cleemann, Dr. R. A.
Clothier, Mr. Isaac
Cohen, Dr. S. Solis
Codman, Dr. C. A. E.
Coley, Dr. Wm. B.
Coley, Dr. F. L.
Cooper, Dr. J. Cardeen
Coplin, Dr. W. M. L.
Cordell, Dr. Eugene F.
Council, Dr. M. S.
Coxe, Mr. Eckley B.
Craig, Dr. A. R.

Craig, Dr. F. A.
Crampton, Dr. G. S.
Crile, Dr. George W.
Cruice, Dr. John M.
Curtin, Dr. R. G.
Curtis, Mr. Cyrus
Cushing, Dr. Harvey

Da Costa, Dr. J. Chalmers
Da Costa, Dr. J. C., Jr.
Daland, Dr. Judson
Dana, Dr. Chas. L.
Darrach, Dr. James
Davis, Dr. E. P.
Davis, Dr. G. G.
Davis, Dr. C. N.
Davis, Dr. William B.
Deaver, Dr. R. W.
Deaver, Dr. John B.
Deaver, Dr. H. C.
Decker, Dr. C. J.
Dehoney, Dr. H.
Dennett, Dr. Wm. S.
Dercum, Dr. F. X.
Despard, Dr. D. L.
Dickey, Rev. Dr. C. A.
Dillard, Dr. H. K., Jr.
Disston, Mr. Jacob
Dorland, Dr. W. A. N.
Dorrance, Dr. G. M.
Dougherty, Dr. S. W.
Downs, Dr. R. N.
Downs, Dr. R. N., Jr.
Drinker, Dr. Henry S.
Duer, Dr. E. L.
Dulles, Dr. C. W.

Eaton, Dr. Albert M.
Edsall, Dr. D. L.
Ellis, Dr. Chas. M.
Ely, Dr. T. C.
Eshner, Dr. A. A.
Estes, Dr. Wm. L.
Erck, Dr. T. A.
Evans, Dr. William

Farr, Dr. Clifford B.
Farr, Dr. William W.
Farrlow, Dr. T. W.
Ferguson, Dr. A. D.
Fetterolf, Dr. George
Fisher, Mr. Charles P.
Fisher, Dr. H. M.
Fitz, Dr. Reginald H.
Fleischer, Mr. P.
Flexner, Dr. Simon
Fordyce, Dr. John A.
Foulkrod, Dr. Collin
Fox, Dr. Herbert
Fox, Dr. Geo. Henry
Fox, Dr. L. Webster
Fraley, Dr. F.
Francine, Dr. A. P.
Frazier, Dr. C. H.
Frazier, Mr. W. W.
Frazier, Mr. Geo. H.
Freeman, Dr. W. J.
Freemann, Roland G.
Friebis, Dr. G.
Friedenwald, Dr. Julius
Furbush, Dr. L. C.
Fussell, Dr. M. H.

Gable, Dr. I. C.
Gamble, Dr. R. G.
Gerhard, Dr. George
Gerrish, Dr. Fred. H.
Gibb, Dr. J. S.
Gibbon, Dr. John H.
Girvin, Dr. John
Githens, Dr. W. H. H.
Gittings, Dr. J. C.
Gleason, Dr. E. B.
Goepp, Dr. R. Max
Goodman, Dr. E. H.
Goodspeed, Dr. Arthur W.
Gordon, Dr. A.
Gordon, Dr. George B.
Graham, Dr. E. E.
Grasett, Dr. F. Le M.
Grayson, Dr. C. P.

Greene, Mr. R. W.
Griffith, Dr. J. P. C.

Hamill, Dr. S. M.
Hand, Dr. Alfred, Jr.
Hansell, Dr. H. F.
Harrison, Mr. C. C.
Hart, Dr. C. D.
Harte, Dr. R. H.
Hartzell, Dr. M. B.
Hays, Dr. I. Minis
Heed, Dr. Charles
Heineberg, Dr. Alfred
Heisler, Dr. J. C.
Henry, Dr. F. P.
Henry, Dr. J. Norman
Hewson, Dr. Addinell
Hibben, Dr. John G.
Higbee, Dr. W. R.
Hirsh, Dr. A. Bern.
Hirst, Dr. B. C.
Hitchens, Dr. A. P.
Hodge, Dr. E. B., Jr.
Hogner, Dr. Richard
Holland, Dr. J. W.
Holloway, Dr. T. B.
Holmes, Dr. E. Burvill
Howe, Dr. Lucien
Hoyt, Dr. D. M.
Hunsberger, Mr. A.
Hunt, Dr. J. Ramsey
Hutchinson, Mr. Sydney E.

Ingham, Dr. J. V.

Jacobi, Dr. Abraham
Jacobs, Dr. H. B.
Jameson, Dr. G. L. S.
Jamison, Mr.
Janeway, Dr. E. G.
Jones, Dr. C. J.
John, Rutherford L.
Johnson, Dr. R. H.
Johnson, Mr. Albo B.
Johnson, Mr. Emory R.
Jopson, Dr. J. H.
Judson, Dr. C. F.
Jump, Dr. H. D.
Jurist, Dr. L.

Kane, Dr. J. A. B.
Keen, Dr. W. W.
Kelly, Dr. J. A.
Kelly, Dr. Howard A.
Kelly, Dr. A. O. J.
Kinnicutt, Dr. F. P.
Knapp, Dr. Philip Coombs
Knipe, Dr. J. C.
Knowles, Dr. F. C.
Kober, Dr. Geo. M.
Kraemer, Dr. Henry
Kremer, Dr. W. H.
Krauss, Dr. Frederick
Krusen, Dr. Wilmer
Kyle, Dr. D. B.

Landis, Dr. H. R. M.
Langdon, Dr. H. M.
Le Boutillier, Dr. T.
Le Conte, Dr. R. G.
Lee, Dr. W. E.
Leiper, Capt.
Leonard, Dr. C. L.
Lewis, Dr. M. J
Lewis, Dr. Dorsey W.
Lindauer, Dr. Eugene
Linthicum, Dr. G. M.
Lippincott, Mr. J. Bertram
Lloyd, Dr. J. Hendrie
Longaker, Dr. D.
Longcope, Dr. W. T.
Lusk, Dr. G.

McBurney, Dr. Charles
McCarthy, Dr. D. J.
McClellan, Dr. George
McFadden, Mr. Geo. H.
McFarland, Dr. Jos.
McKenzie, Dr. R. Tait
McLeod, Dr. Geo. I.
Macallum, Dr. Arch. B.
MacCoy, Dr. A. W.
Mackinney, Dr. Wm. H.
Maier, Dr. F. Hirst

Makuen, Dr. G. H.
Maloney, Mr. Martin
Marple, Dr. W. B.
Marshall, Dr. John
Marshall, Dr. G. M.
Martin, Dr. Edward
Marvel, Dr. Philip
Mays, Dr. Thos. J.
Mears, Dr. J. Ewing
Meigs, Dr. A. V.
Miller, Dr. D. J. M.
Miliken, Mr. B. L.
Mills, Dr. C. K.
Mitchell, Dr. C. F.
Mitchell, Dr. S. Weir
Mitchell, Dr. John K.
Montgomery, Dr. C. M.
Montgomery, Dr. E. E.
Montgomery, Mr. T. H.
Morgan, Mr. Randall
Morris, Dr. Elliston J.
Morrison, Dr. W. H.
Morton, Dr. S. W.
Mosher, Dr. J. M.
Moulton, Dr. A. R.
Muhlenburg, Dr. Wm. F.
Muller, Dr. G. P.
Musser, Dr. John H.
Mutschler, Dr. L.
Myers, Dr. T. D.

Nassau, Dr. C. F.
Neff, Dr. J. S.
Neilson, Dr. T. R.
Newcomet, Dr. Wm. S.
Newlin, Dr. A.
Nicholson, Dr. W. R.
Nolan, Dr. E. J.
Norris, Dr. Geo. W.
Norris, Dr. R. C.

Ochs, Mr. Geo. W.
Odenatt, Dr. W. Burrell
Oliver, Dr. C. A.
Ostheimer, Dr. M.
Ott, Dr. Isaac

Packard, Dr. F. R.
Page, Dr. H. F.
Pancoast, Dr. H. K.
Parke, Dr. W. E.
Parish, Dr. B. D.
Pearce, Dr. R. M.
Penrose, Dr. C. B.
Pennypacker, Hon. S. W.
Pepper, Dr. William
Pfahler, Dr. G. E.
Piersol, Dr. G. M.
Pilcher, Dr. Stephen L.
Pitfield, Dr. R. L.
Polk, Dr. W. M.
Posey, Dr. W. C.
Potter, Hon. Wm.
Potts, Dr. C. S.
Potts, Dr. B. H.
Price, Dr. G. E.
Purves, Dr. G. M.
Pyle, Dr. Walter L.

Randall, Dr. B. Alex.
Randolph, Dr. Robert L.
Reichert, Dr. E. T.
Reyburn, Hon. John E.
Rhein, Dr. R. D.
Rhein, Dr. J. H. W.
Rhodes, Dr. E. G.
Richardson, Dr. Chas. W.
Riesman, Dr. D.
Ring, Dr. G. O.
Risley, Dr. S. D.
Risley, Dr. J. Norman
Roberts, Dr. J. B.
Roberts, Dr. Walter
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RECEPTION IN THE NEW HALL OF THE COLLEGE OF PHYSICIANS, NOVEMBER 11, 1909.

Dr. James Tyson, Introducing Dr. Mitchell.

I know quite well that the orator of the evening needs no introduction to a Philadelphia audience, or, indeed, to any American audience. There is, however, a side of Dr. Mitchell with which you who are not of the profession are less familiar, however much you may know of him as an author and eminent physician. It is that of his relation to the profession of medicine, and what he has done for it, his unbounded love for it, and the pride he takes in its elevation to a higher standard of excellence. This he has shown by losing no opportunity to present its claims to honorable recognition by the community at large, in Municipal, in State, and in National affairs, by personifying its best types in the *dramatis personæ* of his writings, and by generous gifts of money, of rare books, and curios to the College. Everywhere about us we see the evidence of his interest and of his liberality. Without his aid we could not, for a long time at least, have erected this useful and beautiful home, and by him our interest has been kept keenly awake. It is that I might briefly allude to this side of his life, for the information of those who do not know it, that I desired to take advantage of my office to introduce him as our greatest benefactor and as Philadelphia's first and foremost citizen.

ADDRESS OF WELCOME, BY S. WEIR MITCHELL, M.D.

I am honored by the President and Fellows of this ancient collegiate society with the duty of making you welcome to the hospitality of our New Hall.

Few of you who face me now but have known some of your present hosts in hours of anxiety, in a day of release from fear, or at a time when we were made to feel the bitterness of defeat.

You have known us thus as individuals. Here tonight, as a society representative of the science and art of medicine, we greet you, our guests. I find it fitting to say a few words to you Philadelphians of this institution in its relation to the City, the State, and the Country. I hope not to be uninteresting; I promise to be brief.

I am not aware that there has ever been written a history carried through the ages of any one of the learned professions. Most interesting would it be to trace the influence upon the physician of social forms and fancies, religions and governments, to learn how much of his professional characteristics are permanent, how much have undergone a change. It would, I believe, be found that in the Old World the definite boundaries of caste and long settled restrictions kept him for centuries in the bondage of unyielding limitations. He held on his course of progressive advance, but was forbidden by custom to be or to do many things which he might reasonably have desired to be or to do. His social status was unalterably defined.

In some European countries it is today as despotically settled. Even in England—where are many roads which lead to coveted title—only once has a peerage rewarded exceptional achievement in medicine. Nor until of late have sons of the titled classes

been willing to enter my profession. It is all changing for the better, but I doubt a little if the practising physician in Great Britain is as free from the bondage of custom and popular prejudices as are his American brothers.

In the seventeenth and eighteenth centuries, in England, the habits, manners, social place, and even the dress of the doctor were governed by customs which were the more despotic because of being the outcome of the unquestioned legislation of conventional usage. It must have been for some of the men thus fettered a glad day when the tide of immigration flowed westward. It opened a new world of resourceful liberty to the physician. Being usually the most intelligent and best educated of the emigrants, he made ready use of this heritage of freedom. Here in Pennsylvania he was especially fortunate, for by happy accident he was in many instances within the friendship of William Penn, and in some cases of that gentle blood and breeding which did not lose in the new land a certain influential value. These, our earliest physicians, were generally Welsh, and nearly all were of the Society of Friends. Like the great Proprietor, they came hither with the desire to find in this new land that loftiest freedom—the liberty of the worshipping soul. They found also other privileges. In colonial New England the clergy ruled the State. In New York commerce and the landholders were dominant. In the South the planter held sway. In this city, which for a time was the State of Pennsylvania, the physician had in our early days such political and social power as belonged to him as a class nowhere else. The results for him and the Commonwealth were interesting. The small need for medical aid in the young city must have given the doctor much leisure, and that he was selected for offices unrelated to his medical work proves his great superiority to the mass of our early settlers, and was, I think, peculiar to us.

Dr. Thomas Wynne, who came in the "Welcome" with the Proprietor in 1682, was for three years President of that first Legislative Assembly of which Dr. Edward Jones, his son-in-law, was a member. Dr. Thomas Lloyd became Deputy Governor, President of Council, and Keeper of the Great Seal. Dr. Thomas

Graeme, of Scotch descent, a man in large practice, was at one time or another Naval Officer, Master-in-Chancery, and at last Chief Justice, with a salary of $250 a year. He founded our St. Andrew's Society. He aided to create the Philosophical Society, and died Collector of the Port. Dr. Griffith Owen, Penn's physician, was between visits, of the Assembly, a Commissioner of Property, Deputy Master of the Rolls, Coroner, and at last Judge in the Court of Common Pleas. These doctors were variously useful. Dr. John Kearsley planned Christ Church, and, as a legislator, presided over the Assembly.

Dr. Thomas Cadwalader was for years, from 1755, Member of the Council and Assembly, and was also actively useful in making Indian treaties and in arranging fortifications for the defence of the city. The physician of the first half of the eighteenth century was the busy founder of schools, hospitals, colleges, learned societies and libraries. It is in some respects a singular story, of which with justice we are proud; it should be more fully told. At a later day Benjamin Rush was a signer of the stern arraignment of the Crown and during a life of vast industry a member of almost every legislative body up to the time of his death. Dr. William Shippen, too, was of the Continental Congress. I may add that, besides the many lawyers who signed the Declaration of Independence, there were five men who had practised medicine.

I have desired to make clear to you how large was the life of the physician in this city during the eighteenth century. No social fetters hindered him; no clogging traditions forbade him personal independence. Nowhere else, in any land, had the doctor asserted his freedom as a man to do what he pleased, if only as a physician he did with thoroughness the medical business in which the public found use for him. It is so to this day, as some of us most thankfully know. To men like these we of this city owe, with much else of as permanent value, the foundation of this Collegiate Society. It is, therefore, fitting that we have asked hither tonight what is most representative of the historic and social life of Philadelphia, to remind you of what this institution is today and has been in the past.

And now go back with me to the birthday of this College. Philadelphia had then some 40,000 people. It was the seat of Government. Franklin, Bartram, and Rittenhouse represented its science. Washington, at fifty-six, was then of the troubled men who were in this year to forge the constitutional bond destined to be the parent of so much good and to sow in its indecisions the seed of so much bloodshed.

In the Academy building, on Fourth Street, south of Arch, then in use by the University of Pennsylvania, on the evening of January 2, 1787, assembled a notable group of men. I seem to see these ruddy gentles by the dim light of the candles, for which I find our first bill of 2*s.* 6*d.* There are some in Quaker beavers, and all are in knee breeches and stockings, with gold buckles, or silver, on the low shoes, good lace neckgear and wrist ruffles. The powdered wig is here—a fading fashion. They sat, I am sure, with between their legs the professional gold-headed cane. Now and then, to aid their deliberations, they consulted the meditative snuff-box. I find, too, a receipted bill, 11*d.*, for a bushel of sand—I presume to cover the floor.

In this old building Whitfield preached. To the east, across the street, was the Quaker burial ground. To the west was the graveyard of Christ Church. In one or other of these final homes nearly all of these men were to find at last repose. Some wit was wasted on the doctors in consultation between two graveyards.

I want to connect these, our own ancestors, with the family history of the city. It is almost enough to mention the names of these men. They sound familiar as the hour, for here with us wealth has not been essential to keep families in the social foreground of repute.

Of the founders of this Society were John Jones, Benjamin Rush, William Shippen, Adam Kuhn, James Hutchinson, Gerardus Clarkson, John Redman, George Glentworth, Samuel Powel Griffiths, John Morris, John Carson, John Foulke, and, later, Michael Leib, Caspar Wistar, Parke, Dorsey, and others.

Let me add their medical ancestors and teachers: Wynne, Jones, Graeme, Cadwalader, Griffith, Owen, Bond, Lloyd, and the elder

John Kearsley. A long roll of our city families trace their descent from members of these memorable groups. Of our own founders were many who assisted at the birth of the nation, rode with Washington, and shared the fates of indecisive battles and the privations of Morristown and Valley Forge.

As soldier-surgeons they knew the national neglect which rewarded the services of the army doctor of our later history. It is no pleasing thing to confess that no monumental marble tells of the gallant gentlemen who were heroes of Surgeon Reed's immortal victory over yellow fever. What record is there of the surgeons who fell on many battlefields in our Civil War? They died while aiding the wounded, or were killed while calmly operating under fire where bullets were raining death. What test of courage compares to that? The land is populous with statues of generals, some of whom are ever most gratefully to be remembered, some of whom it were as grateful to forget. No such memorials record the country's gratitude to the surgeon-soldier– that essential partner in the terrible business of war.

Look around you in this noble hall. We at least do not forget. Here are portraits of the physicians who were friends of Washington, Franklin, Lafayette, and Hamilton. I should like to have been physician to Hamilton! The portraits of our Presidents are here, from John Redman, in 1787, of whom it was said that "by his soothing manner he suspended pain, or chased it away by his conversation." I fear the secret of this anesthetic manner is lost today. I should like to linger over these notable personalities, our founders. Rush would need too large a page. Most of them are well known. Some have but a brief record; thus Glentworth, whose history is in a line of a letter of Washington. He says of this, his surgeon Glentworth: "No nobler man or more skilful physician ever lived—an estimable friend." With such brief judgments I could sum up for you how these men were considered in their own day. They seem, indeed, very near to us when, for instance, we come upon Caspar Wistar, whose name, given in his honor to the beautiful vine Wistaria, is heard in every country. Of him it was said: "Decorous, suave, honorable, and courteous, he forgot nothing except injuries."

Many of our pictures of the men of a more recent time must for some who are here tonight call up grateful memories.

I remind myself and you that this is the new home of a Philadelphia institution nearly a century and a quarter old. It was felt by us that it should be something more important, more monumental, than merely a place for our meetings and our great Library.

Of this last a word is needed. As you wander you will come at the back of the hall upon the iron book stacks which guard 89,000 volumes and 100,000 pamphlets. An absolutely free Library, it is open to all who would read here. A card from a Fellow gives permission as freely to take books home. Here come and are welcome men and many women, physicians of every sect, reporters, the laity, in search of knowledge of spas, climatic conditions, and other matters of interest. What this vast collection is to us, how essential, I need not say. It preserves for us the changing story of our history, and we are kept in constant touch with the science of all nations by the receipt of 900 journals.

Let me now ask your attention to our performance of another important public service in our Directory for Nurses. I am pleased to say that the fee formerly asked for furnishing a nurse is now abolished. The Directory is to-day as free as is our Library. It is simple. A telephone call brings a nurse to the bedside. You may get some idea of the vast usefulness of this service when I tell you that since 1882 the Directory has answered over 43,000 requests for trained nurses. Pray understand that no charge is made for furnishing a nurse.

This hall was meant to be also a monument commemorative of men who served alike their city, their country, and their God. It is yours in this sense. It is also ours. Some of the rooms which bear names you share or with which you have ancestral connection are furnished by families as memorials of their medical forefathers.

Within and without, nothing in the way of taste-guided thoughtfulness has been spared to make this building an ornamental addition to the city. It owes its unusual architectural charm to

the skill of Messrs. Stewardson & Jamieson, to whom I gladly offer the thanks of the College; as warmly I thank the members of the Building Committee, who have given to every detail an incredible amount of industry, time, and thought.

To this, our new home, we welcome you tonight.

This building could not have been built for years had it not been for the generous gifts not only of our citizens, but of friends elsewhere, who understood that the history of medicine in this city is national property. To speak rightly of those who gave would be only to insist that the giver of $5 may be on an equality of generous expenditure with the giver of $100,000. The list of subscribers, soon to be printed in the record of our present commemoration, will gratefully mention all who gave. Of them, were nearly all the Fellows of the College.

I end with but one regret. We enter our new home with a certain amount of debt. I do not doubt that in this audience are Philadelphians who will find pleasure in the opportunity to aid us in meeting this obligation.

The President and Fellows will now receive you, our friendly guests.

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ŒDEMA.[1]

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I. THE PROBLEM.

The pages that follow concern themselves with a problem in clinical pathology which upon its face bears every evidence of simplicity, which in essence no doubt is as simple as it looks, but which has nevertheless yielded small and unsatisfactory returns to the men who have labored toward its solution. A moment's reflection may show why this has been the case.

The problem of œdema—the problem of the presence of abnormally large amounts of water in tissues and tissue spaces—is essentially only a phase of that greater problem: Why protoplasm holds any water at all, and why it holds under normal circumstances so nearly constant an amount. It is easily seen why an interest in œdema should have overshadowed the greater and really simpler problem, for œdema has a human interest that is entirely lacking to the question of why protoplasm generally holds water. That attempts should in consequence have been made to answer the question of œdema first is not surprising. The ways and means adopted may, however, well serve as an example of the short-cut methods which clinicians and pathologists have only too often adopted in order to obtain light, and with disastrous results. Since œdema constitutes a pathological state

[1] The 1909 Nathan Lewis Hatfield Prize Essay of the College of Physicians of Philadelphia.

of interest chiefly in man, various hypotheses were formulated to account for the condition on the basis of his complex anatomy—such, for instance, as his circulatory system; and when experiments on the higher animals failed to bring the corroborating evidence which should convert the shadowy hypothesis into the healthy theory, recourse was had to the still more shadowy properties of "living" cells. And to this day the accepted explanation of œdema is still an ill-defined mixture of the physical concepts of pressure and filtration with the mysterious forces of living matter.

A little thought will show that variations in the amount of water held by cells and tissues—variations analogous to a state of œdema in vertebrates—occur in a great variety of animals and plants. To cite but a single example, and one common to both plants and animals, mention may be made of the widespread plasmolytic phenomena. Under a variety of circumstances single cells may be made to absorb enough water to burst. These are "œdemas" as true as any ever observed in man, or produced experimentally in a dog or rabbit. Such reflection should by itself have created suspicion against any conception of œdema which demands for its production a circulatory system or any structures not common to *all* protoplasm, vegetable as well as animal.

It will not seem strange after what has been said that the best contribution toward the solution of the problem of the ways and means by which cells and tissues absorb water has in recent years really come through the plant physiologists. Not led into erroneous paths through the presence of circulatory systems at all similar to those found in the higher animals, the plant physiologists early sought the explanation of the variations in the amount of water held by the plant tissues in the cells themselves. As we shall see very shortly, this is where the problem belongs, and the attempts of later years to make differences in osmotic pressure responsible for the movement and storage of water in animal cells as well as in plant cells under normal and pathological conditions cannot be too highly commended. While the theory

of osmotic pressure is incapable of accounting for more than a small portion of the phenomena observed—even in plants—the great value of an attempt to explain variations in the water content of animal and plant tissues on a healthy physico-chemical basis cannot be questioned.

To a consideration of the various hypotheses and theories which have been proposed to account for œdema we shall have occasion to return later. We will give our attention first to a series of experiments which prove conclusively that *the cause of œdema resides in the tissues*. After this has been done we shall attempt a physico-chemical analysis of the forces active in the process.

II. THE CAUSE OF ŒDEMA RESIDES IN THE TISSUES.

A very simple experiment proves this fact. If one leg of an ordinary frog (Rana), a tree frog (Hyla), or a toad (Bufo) is ligated just above the knee as tightly as possible, so that the ligature shuts off not only the venous flow, but also the arterial, and the animal is then placed in sufficient distilled water to cover the legs, *the ligated leg develops an intense œdema*, while the unligated one remains normal. To explain this result recourse cannot be had in this experiment to the pressure of any circulating liquids, for none such exists, and so *all the conceptions of œdema which regard the pressure, per se, of circulating liquids, as one of the causes, or the chief cause, in the development of this condition, are robbed of their most fundamental support.*

The choice of animals for these experiments was not entirely a random one. It seemed especially desirable to deal with an animal in which there exists normally an outside source of water for the tissues, one separate from the ordinary blood or lymph current. Such conditions are satisfied in any of the amphibians. It would seem, nevertheless, that the absorption of water may be obtained through the skin of all animals, for my toads developed just as intense œdemas of the leg as did the frogs, and it is a well-

known fact that the bodies of dead land animals swell (become œdematous) if kept in water.[1]

The œdemas which these frogs and toads develop are in every way a counterpart of the most intense forms observed clinically. The tissues are boggy, pit on pressure, and when incised allow the escape of fluid.

The rate at which the œdema develops in these three kinds of animals is not the same in all. It develops and passes away most rapidly in tree toads (Hyla). For toads (Bufo) and ordinary frogs (Rana) the following holds: An œdema of the ligated leg is readily discernible at the end of eighteen hours, and is very marked at the end of twenty-four. Within forty-eight hours the swelling approaches its maximum, and may at times be so great that the skin of the ligated leg is ruptured. This maximal swelling is usually maintained some two days, when it begins to diminish, and the leg gradually tends to assume its original size.

The diminution in size is at first merely due to a loss of water, dependent upon changes in the tissues which we shall discuss later. But in the entire absence of a circulation the leg below the ligature cannot, of course, continue to live, and so anywhere from one to two weeks after the ligature has been tied, the skin peels and splits and the tissues below it become soft and disintegrate. This loss of substance becomes progressively greater until at the end of three to five weeks only a bony stump covered with tags of tissue may be left.

A number of accessory phenomena are deserving of mention. Twenty-four to forty-eight hours after the ligature has been tied a number of small vesicles usually begin to develop upon the œdematous leg. They are found earliest and most commonly in the tissues of the web of the foot, but they may occur anywhere in the skin below the ligature. The small vesicles which appear early, gradually increase in size until forty-eight to ninety-six

[1] It is needless to point out that the *bloating* of bodies in consequence of the development of *gas* through bacterial action in the gastro-intestinal tract or in the tissues proper is of course not referred to in this remark.

FIGURE 2

Fig. 3

Figure 5

hours after the ligature is tied they become great blebs, which in place of the original water-white or faintly straw-colored fluid found in the vesicles are likely to contain (especially in toads) a blood-stained serum. After these have persisted a day or two, they rupture and allow the escape of their contents.

The color of the skin of the ligated legs also suffers change. Within twelve hours after the ligature is tied this is usually seen to fade somewhat, and to lose the lustre of the healthy skin. At the end of forty-eight hours the color markings, characteristic of the particular species of frog under observation, are always much blurred. Late in the experiment (in the second or third week), the ligated leg assumes the gray or grayish-black look of necrosis.

What has been said is illustrated in Figures 1, 2, 3, 4, and 5. Figure 1 is a photograph of a frog (Rana), kept in a little water, forty-seven hours after a ligature has been tied as tightly as possible about the left leg. The increase in the size of this leg over the normal right is clearly apparent. Figures 2 and 3 illustrate the same fact in another frog treated the same way. The tense skin with the blurring of surface markings is easily noted in all three pictures. Later photographs of the frog of Figure 1 are shown in Figures 4 and 5. These were taken ninety-five hours after the ligature was tied. Some small blisters which formed between the toes have increased in size to constitute the large bleb seen in the photographs. The œdema in the leg and foot generally is still evident.

While these photographs show us clearly that an œdema develops in a frog's leg even in the total absence of a circulation, they tell us nothing of the severity of these œdemas; in other words, simple inspection of the illustrations does not yield conclusive evidence that the œdemas are as severe as any ever observed clinically. To settle this point it will be well, therefore, to insert the protocols of a few experiments in which the œdematous legs were amputated at various periods after the ligature had been tied and their weight compared with that of the normal leg of the opposite side.

Protocol I (December, 1907).

One leg is ligated with a silk ligature just above the knee in each of four *toads* (Bufo), and the animals are placed in separate dishes, each containing enough distilled water (50 c.c.) to cover the legs. The ligated legs are found visibly œdematous at the end of twenty hours. The toads are left in the dishes for fifty-four and one hundred and sixty-eight hours, when they are killed, and the two legs are amputated (the ligated one just above the ligature and the other at a corresponding point on the opposite leg), and weighed. The difference in weight, with the gain on the part of the ligated leg expressed in percentage of the weight of the unligated leg, is shown in the table.

54 hours, A { Ligated, 0.436 (+26.01%)
Unligated, 0.346 (0%)

54 hours, B { Ligated, 0.371 (+25.33%)
Unligated, 0.296 (0%)

54 hours, C { Ligated, 0.444 (+45.09%)
Unligated, 0.306 (0%)

168 hours, D { Ligated, 2.152 (+82.37%)
Unligated, 1.180 (0%)

Protocol II (March, 1908).

A ligature is tied as tightly as possible just above the knee about the left hind leg of six *toads* (Bufo). The toads are placed in finger bowls containing 100 c.c. distilled water. After varying periods they are taken out, killed, and the weights of their hind legs compared as already outlined. The results are given in the table.

4.30 hours, A { Ligated, 1.080 (+33.33%)
Unligated, 0.810 (0%)

17.30 hours, B { Ligated, 3.350 (+58.01%)
Unligated, 2.120 (0%)

28.00 hours, C { Ligated, 4.137 (+80.26%)
Unligated, 2.295 (0%)

43.45 hours, D { Ligated, 7.840 (+56.17%)
Unligated, 5.020 (0%)

53.00 hours, E { Ligated, 7.262 (+130.39%)[1]
Unligated, 3.152 (0%)

124.45 hours, F { Ligated, 7.160 (+23.23%)
Unligated, 5.810 (0%)

[1] The toes of the sound leg are missing. The œdematous leg is practically covered by very large blebs.

A

B

Figure 6

The foregoing experiments prove conclusively that the severest grades of œdema may develop in toads and frogs in the entire absence of a circulation. It is next in order to consider the objections which may be and have been raised against these experiments. All of these objections come to this, that in spite of the ligature some sort of a blood or lymph circulation with its ever adherent "pressure" still exists in the leg. One should, of course, be entirely convinced that no ordinary circulation can continue through the soft tissues of the leg when it is remembered that the ligature is tied as tightly as possible about the leg at a point where musculature is practically lacking. The only other possibility for a circulation would have to be found through the lower end of the femur, and the tissues in and about the knee-joint, whereby a connection between the thigh above, and the leg below, might be conceived to be continued. These objections are answered by two facts: (1) *If the ligature is tied about one leg of a frog, and the animal is not kept in water, but in a dry vessel, the ligated leg dries up entirely, and this member is carried about in a mummified condition for as long as the experiment is continued, and may finally be broken off and so lost.* The rest of the frog dries out much more slowly than the ligated leg. (2) *If after ligating the leg the member is amputated and placed in a little distilled water, this amputated member shows the same series of changes as though it had been left united to the frog.* We will find abundant evidence of this fact in the experiments to be described later. Ocular demonstration of this fact may be found in Figure 6. In this are shown anterior and posterior views of two frogs' (Rana) legs forty-nine and one-half hours after they had been ligated, amputated, and placed in distilled water. The spreading toes, bulging webs, and swollen leg muscles mark the œdema. How great this is is still more apparent when it is stated that the larger leg has gained 51 per cent. in weight, while the smaller one has gained 50.2 per cent. It would be difficult to conjure up the existence of any orthodox circulation in this experiment with amputated legs.

The two protocols that follow may serve in further illustration

of what has been said. In these, tree toads were used. Similar experiments with frogs will be found further along in this paper, and need not be dealt with separately here.

Protocol III (December, 1907).

A ligature is passed about the left leg above the knee in each of two *tree toads*. The one toad is kept in a dry vessel, the other in one containing a little distilled water. Twenty hours later, œdema is well marked in the ligated leg of the frog kept in water, while the ligated leg of the frog kept dry is already beginning to shrivel. At the end of fifty-eight and one-half hours the toads are killed, the legs amputated and weighed, with the following results:

A, kept dry { Ligated, 0.071 (—38.8%)
Unligated, 0.116 (0%)

B, kept moist { Ligated, 0.279 (+78.8%)
Unligated, 0.156 (0%)

Protocol IV (June, 1908).

Three *tree toad* legs are obtained by amputating them close to the pelvis. The skin is pulled over the femoral stump in each of the preparations and ligated tightly. They are then weighed and placed in separate finger bowls containing 110 c.c. distilled water each. The first number in each of the columns gives the weight of the tree toad's leg at the beginning of the experiment. After each of the weighings is given in parenthesis the percentage of increase in weight, over the original weight of the muscle.

Hours in solution.	110 c.c. H_2O.	110 c.c. H_2O.	110 c.c. H_2O.
0.	0.486 (0)%	0.473 (0)%	0.363 (0)%
0.30	0.560 (+15.2)	0.540 (+14.1)	0.417 (+14.8)
1.30	0.600 (+23.4)	0.590 (+24.6)	0.465 (+28.1)
2.30	0.630 (+29.6)	0.620 (+31.0)	0.498 (+37.2)
4.30	0.712 (+46.5)	0.703 (+48.6)	0.557 (+53.4)
6.10	0.795 (+63.5)	0.770 (+62.8)	0.620 (+72.7)
17.35	0.944 (+94.2)x	0.799 (+68.9)x	0.662 (+82.3)x
22.25	0.842 (+73.2)	0.772 (+63.2)	0.627 (+74.7)
28.45	0.780 (+60.5)	0.755 (+59.8)	0.598 (+64.7)
	d	d	

d, d, represent opposite legs of the same toad
x. At this point the legs are found blistered.

Figure 7 is based upon the calculations contained in Protocol IV and represents graphically the course of water absorption as observed in these three amputated tree toads' legs. The curves show that the initial increase in weight is followed later by a decrease. This corresponds with the ocular observations already detailed on the development of œdema in ligated legs left in situ, which at first gradually increases in severity until a maximal point is reached, after which the œdema lessens.

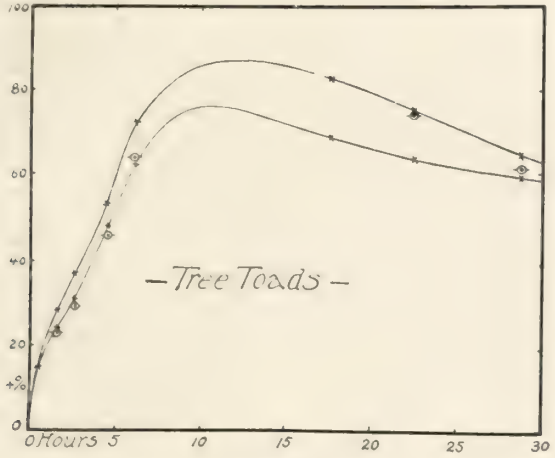


FIGURE 7

After what has been said it will not seem strange that these œdematous changes in a ligated leg occur in a toad or frog just as readily and rapidly if the animal is pithed as when this is not done. If, however, the animal dies, the difference between the weight of the two legs does not develop. This is not, however, because the œdema does not develop in the ligated leg—it does just the same—but *an equally intense absorption of water occurs in the other leg which through the death of the animal has been deprived of its circulation.*

From the experiments that have been described it is very clear that the most intense states of œdema may develop in an animal in the entire absence of any circulation. We are, therefore, already

able to cast aside those explanations of œdema which attribute the development of this state to the pressure of circulating liquids. *It is clear that the cause of œdema resides in the tissues themselves, and that these become œdematous not because water is forced into them, but because changes take place in them whereby they are enabled to absorb water from any available source.* In the case of the experiments on toads and frogs this available source of water is the water contained in the dishes in which the animals are kept. In clinical cases of œdema, this is found in the fluids which pass through or about a tissue.

In the succeeding sections of this discussion we will obtain further evidence to show that the cause of œdema resides in the tissues. We will see that what holds for frogs' legs holds also for isolated muscles, for the kidney, the liver, and for the eye.

Let us first try to discover what are the changes that take place in any tissue in order that it may become œdematous. As I regard changes in the colloids of the tissues as of primary importance in this connection, it is necessary, first of all, to review briefly some of the properties of colloids, with particular reference to their behavior toward water.

III. REMARKS AND OBSERVATIONS ON COLLOIDS.

1. Remarks on Colloids: Nomenclature.

It is now more than fifty years since Graham recognized that different chemical substances differ greatly in the rate with which they diffuse through solvents of various kinds. On the basis of this observation he made a distinction between those which diffuse only slowly and those which diffuse very rapidly. As the former are for the most part amorphous, and since ordinary glue is an example of this class, he called them colloids. The group that diffuse readily he called crystalloids, for such beautifully crystalline substances as cane sugar, ordinary salt, and urea are found in it.

Since Graham's studies we have become familiar with further characteristics of colloids and crystalloids. Crystalloids are ordinarily stated to form true solutions. This, colloids do not—they form pseudo-solutions, that is to say, they simply remain suspended in the solvent. Colloidal solutions are, therefore, not homogeneous, but heterogeneous in their make-up.

Solutions of crystalloids show an osmotic pressure, which is proportional to the number of particles of dissolved substance in the unit volume of the solvent. Upon this fact and the minuteness of the dissolved particles depends the diffusibility of the crystalloids. The most typical colloids, on the other hand, show practically no osmotic pressure, and correspondingly no diffusibility.

The enormous differences in osmotic pressure between crystalloids and colloids correspond to similar differences in the molecular weight of the substances composing the two groups. The molecular weight of the most pronouncedly colloidal bodies may be measured in thousands, while two or three hundred covers the weight of even very complex organic compounds.

It must be stated at once, however, that between the two extremes of the typical colloids, and the typical crystalloids, there is found an infinite number of substances which lean more or less strongly toward one side or the other. It is possible, for example, to obtain in a crystalline form, certain albumins which may ordinarily be taken to represent our most typical colloids. Egg albumin may be obtained in such a state, and the physiological chemist is rarely satisfied with a hæmoglobin that is not beautifully crystalline. On the other hand, comparatively simple bodies, such as silicic or tungstic acids are found in the group of our most representative colloids. These few facts will suffice to show that no hard and fast line can be drawn between the colloids on the one hand, and the crystalloids on the other.

It should be clearly understood that while we speak of colloids and crystalloids, and, therefore, are seemingly classifying *substances*, we ought really to speak only of the colloidal and crystalloidal *state*. Our familiar use of the terms colloid and crystalloid

has grown out of the fact that certain chemical compounds are best known to us in the colloidal state, while others we see almost always in a crystalloidal state. As a matter of fact, it is probably safe to assume that *any* substance may be obtained in a colloidal form, even those simplest and most typical crystalloids, the chlorides of the various metals.

That many typical colloids may, on the other hand, be obtained in crystalline form is evidenced daily by the ever growing list of biological products long known to us only in the form of amorphous powders, mucilages, and syrups which chemists are obtaining in crystalloidal form. These considerations are not without biological significance, for a chemical substance in a colloidal form may and usually does possess entirely different properties from the same chemical substance in a crystalloidal form. This fact has been abundantly proved within the last decade in many striking ways. The question of *how* a crystalloid passes over into the colloidal form, or vice versa—a question which has as yet been scarcely investigated physico-chemically—is, therefore, of the greatest importance to biological chemistry, for these very conversions of colloids into crystalloids, and crystalloids into colloids, are among the commonest observed in the living organism. The question of glycogen formation from dextrose, for example, represents such a change. Coupled with the chemical change of a dehydration there is in this case a physical change which converts a freely soluble, osmotically active, diffusible crystalloid, into an insoluble (pseudo-soluble), osmotically inactive, non-diffusible colloid.

Marked as are these general differences between colloids and crystalloids (the colloidal and the crystalloidal state), the colloids themselves do not all possess the same properties. Because of this, various attempts have been made to classify the colloids, but it cannot be said that these classifications have been entirely satisfactory. Not only do colloids differ from each other in very essential qualities, but one and the same colloid may exist in two or even more states. As this paper deals particularly with the relationship existing between colloids and the water they hold,

the distinction that A. A. Noyes[1] has made between those colloids which are viscous, gelatinizing, and not readily coagulated by salts (colloidal solutions) and those which are non-viscous, non-gelatinizing, and readily coagulated by salts (colloidal suspensions) is of great interest for our purposes. To the former of these groups belongs, for example, a solution of gelatine, glue, or dextrin, while in the latter might be mentioned the colloidal solutions of ferric hydroxide, aluminium hydroxide, and of various metallic sulphides.

What amounts for our purposes to a very similar classification is that of Perrin,[2] who distinguishes between those colloids which in the solid state are rich in water and those which are poor. The former of these Perrin designates as *hydrophilic* colloids; for the latter the name *hydrophobic* colloids has been suggested. For the purposes of biology these terms are excellent, and in large part adequate. For the purposes of physical chemistry in general they have the drawback of not being sufficiently broad. Water is not, of course, the only solvent that may form the base of a colloidal solution.

Wolfgang Ostwald,[3] who has taken a valuable step forward in the proper classification of the various colloids, distinguishes between the *emulsion colloids* and the *suspension colloids*. The former represent colloidal solutions formed through mixture of two liquid phases, the latter through the mixture of a solid with a liquid phase. A separation of the two phases is difficult to obtain in the emulsion colloids which correspond, it will be seen, with Noyes' first group and Perrin's hydrophilic colloids, while the ready separation of the phases in Ostwald's second group brings to mind Noyes' second group, and the hydrophobic colloids.

When we recall that the hydrophilic colloids which have thus far been accorded most study — gelatine, dextrin, starch, glue, vegetable fibers, albumin, gums — are for the most part derived

[1] Journal of the American Chemical Society, 1905, xxvii, 85.
[2] Journal de Chimie Physique, 1905, iii, 50.
[3] Zeitschr. f. Chemie u. Industrie d. Kolloide, 1907, i, 291 and 331.

from biological sources their probable importance to the living animal or vegetable must at once be suspected. Not only is the chief mass of the living organism built up of colloidal material, but most of it belongs to the hydrophilic group. We will not be surprised, in consequence, to find that that physico-chemical characteristic which makes for the division of all colloids into two great classes will show itself of importance in determining the behavior of the tissues toward water.

It will give us a better conception of just what this absorption of water by colloids represents, and how it is influenced through various external conditions, if we study for a moment the swelling of fibrin.

2. Observations on the Swelling of Fibrin.

In these experiments ordinary blood fibrin was used, which after having been thoroughly washed to free it from adhering salts was dried at a low temperature and pulverized in a mortar. When weighed amounts of such powdered fibrin (0.25 gram) are introduced into definite volumes (25 c.c.) of various solutions contained in test-tubes of the same diameter (1.7 cm.) the fibrin swells to very different heights. From the results of many series of experiments, the following facts which are of importance in our discussion have been determined.[1]

(*a*) Fibrin swells more in the solution of any acid than it does in distilled water, but when equinormal acids are compared, the amount of this swelling is found to be greater in some acids than in others. To mention in particular only a few of a whole series of acids that have been studied, it is found that fibrin swells more in hydrochloric acid than in nitric acid, and more in this than in acetic acid. Even less capable than the last named is sulphuric acid, in whose solution fibrin swells but little more than in distilled water.

[1] See also Martin H. Fischer and Gertrude Moore, American Journal of Physiology, 1907, xx, 313; Zeitschr. f. Chemie u. Industrie d. Kolloide, 1909, v, 197; Martin H. Fischer, Pflüger's Archiv f. d. ges. Physiologie, 1908, cxxv, 99.

The amount that fibrin swells in any acid solution is dependent upon the concentration of the acid. Within certain limits fibrin swells the more the higher the concentration of the acid. In the case of the "strong" acids, however, a maximum is attained, above which a further increase in the concentration of the acid does not lead to a greater absorption of water, but to a diminished one. These facts are well brought out in the following table, which may serve as an illustration of the values obtained in such experiments as are being described. In the case of acetic acid it will be noted that the highest concentration of acid used in the table induces the greatest amount of swelling. At concentrations above $\frac{1}{10}$ normal I obtained a height up to 41 mm. with this acid. As yet I have not, however, been able to determine if with such a "weak" acid a point is finally reached beyond which, as with the "strong" acids, a further increase in concentration brings about a diminished absorption.

TABLE A.

Concentration of the acid.								Height of the fibrin column in mm. after 24 hours in			
								Hydrochloric acid.	Nitric acid.	Acetic acid.	Sulphuric acid.
1	c.c.	1/10	normal	acid	+24	c.c.	H_2O	12	13.5	8.5	8.0
2	"	"	"	"	+23	"	"	23	26.0	10.0	9.0
3	"	"	"	"	+22	"	"	37	29.0	10.5	9.5
4	"	"	"	"	+21	"	"	47	37.5	11.0	10.0
5	"	"	"	"	+20	"	"	48	35.0	12.0	10.0
6	"	"	"	"	+19	"	"		30.0	12.0	11.0
7	"	"	"	"	+18	"	"		30.0	13.0	11.0
8	"	"	"	"	+17	"	"		25.0	13.0	10.0
9	"	"	"	"	+16	"	"		23.0	14.0	10.0
10	"	"	"	"	+15	"	"	41	21.5	14.5	10.0
12-1/2	"	"	"	"	+12-1/2	"	"		18.5	15.0	10.0
15	"	"	"	"	+10	"	"	31	17.0	16.0	9.0
17-1/2	"	"	"	"	+ 7-1/2	"	"		14.5	17.0	9.0
20	"	"	"	"	+ 5	"	"		14.0	18.0	8.5
25	"	"	"	"	. . . . .			21	11.5	18.5	8.5
25	"	water	(control)					8	8.0	8.0	8.0

b. Fibrin swells more in the solution of any alkali than in pure water, but the amount of this swelling is greater in some alkalies than in others. This statement is the analogue of the

corresponding one for acids. When equinormal solutions are compared fibrin swells more in potassium hydroxide than in sodium hydroxide, and more in either of these than in calcium hydroxide or ammonium hydroxide in the order named. Just as in the case of acids so here also is the amount of swelling dependent upon the concentration of the alkali. Within certain limits there is an increase in the amount of swelling with every increase in the concentration of the alkali, but after a certain point is exceeded a further increase in concentration is followed by a diminution in the height of the fibrin column.

(*c*) If the amounts that fibrin will swell in acid and alkali solutions having the same H or OH concentration are compared it is found that fibrin swells much less in the solution of an acid than in an equally concentrated solution of an alkali. While, for example, in a $\frac{1}{5}$ normal KOH or NaOH solution, the fibrin column may be found to measure 83 and 77 mm. respectively, in a $\frac{1}{5}$ normal HCl or HNO_3 solution it measures only 48 and 35 mm.

(*d*) We come now to the interesting fact that the addition of any salt to the solution of an acid or an alkali decreases the amount that fibrin will swell in that solution. The only exceptions to this rule are formed by the salts which react with the acids. If barium chloride, for example, is added to a sulphuric acid solution, the amount of swelling is not decreased, but increased. This is because the insoluble barium sulphate is produced and thrown down, while hydrochloric acid is formed in which fibrin swells more than in an equally concentrated sulphuric acid solution.

The higher the concentration of the added salt, the less does the fibrin swell, and if enough is added the effect of the acid or alkali may be suppressed entirely.

(*e*) If the effect of equimolecular salt solutions is compared, it is found that they affect the swelling of fibrin in solutions of acids or alkalies to very unequal degrees. This is readily apparent from Figure 8, in which is shown the effect of adding various potassium, strontium, and uranium salts to a hydrochloric acid solution. Each of the solutions with the exception of the control,

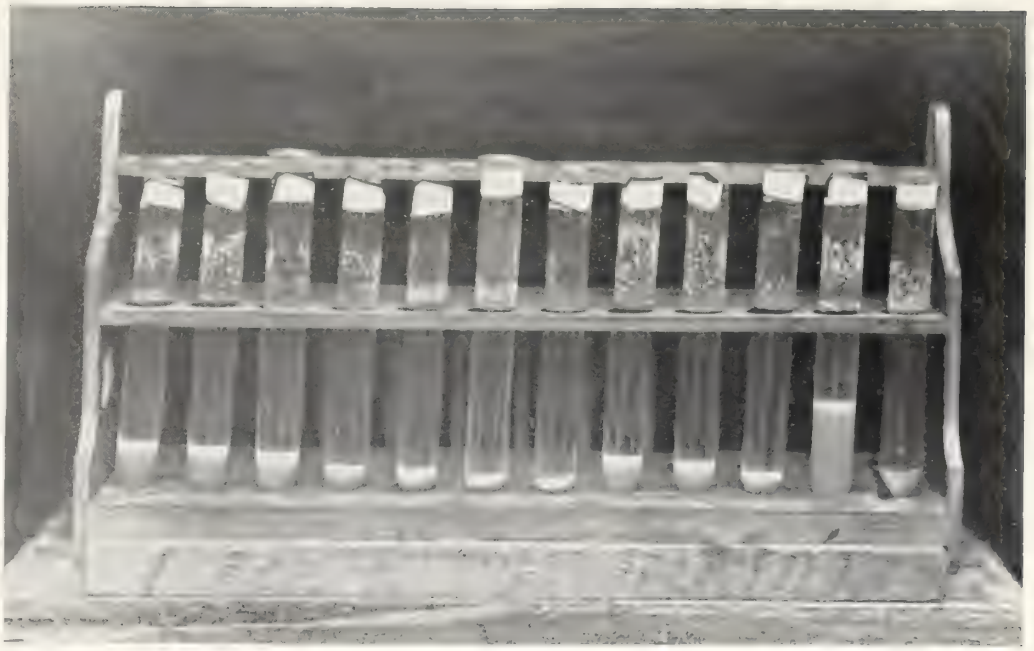


Figure 8

FIGURE 9

which contains $\frac{1}{4}^0$ normal acid only, is so arranged that when finished it contains a $\frac{1}{4}^0$ molecular solution of the salt in a $\frac{1}{4}^0$ normal solution of hydrochloric acid. Reading from left to right, the test-tubes contain the following solutions: The first seven contain hydrochloric acid plus, respectively, the chloride, bromide, nitrate, iodide, acetate, sulphate, and citrate of potassium. The next three contain hydrochloric acid plus the chloride, bromide, and nitrate of strontium. Next to last in the series is a pure hydrochloric acid solution. The last tube contains the same concentration of acid plus uranyl nitrate. Similar relationships are found in Figure 9, where the effect of adding molecularly equivalent amounts of various sodium salts to a hydrochloric acid solution is portrayed. The tube on the extreme right contains pure hydrochloric acid ($\frac{1}{4}^0$ normal). From right to left the succeeding tubes contain the same amount of hydrochloric acid plus various sodium salts ($\frac{1}{4}^0$ normal HCl in $\frac{1}{4}^0$ molecular salt solution). The salts added from right to left are respectively the chloride, bromide, nitrate, acetate, tartrate (of sodium and potassium), sulphate, citrate, and phosphate of sodium. The last tube on the extreme left contains pure water as a control.

The tube on the extreme left in Figure 10 contains a pure $\frac{1}{4}^0$ normal solution of sodium hydroxide. It will be noted that the fibrin column stands higher in this tube than in those of Figures 8 and 9, which contain the pure $\frac{1}{4}^0$ normal hydrochloric acid. The remaining tubes of Figure 10 show the effect of adding molecularly equivalent ($\frac{1}{4}^0$ molecular) amounts of various sodium salts to the pure sodium hydroxide solution. From left to right the salts added are the bromide, nitrate, acetate, tartrate, sulphate, citrate, and phosphate of sodium.

From the study of many series of salts it has been found that the effect of any salt is made up, in major part at least, of the sum of the effects of its constituent ions. In any series of salts having a common kation the order in which the anions are effective is always found to be the same, and when series having a common anion are compared, the order in which the kations are effective is always the same. As a result of these experiments, the follow-

ing two tables have been constructed. The ion least effective in bringing about a diminution in the amount that fibrin will swell in the solution of any acid or alkali is in each case placed first:

Anions.	*Kations.*
Chloride	Potassium
Bromide	Sodium
Nitrate	Ammonium
Sulphocyanate	Magnesium
Iodide	Calcium
Acetate	Barium
Sulphate	
Phosphate	Strontium
Tartrate	Copper (ic)
Citrate	Iron (ic)

The table for the anions is more accurate than the table for the kations. This is dependent upon the fact that the amount of difference in swelling produced by the end members of each of the two series is decidedly greater in the case of the anions than in the case of the kations. The general grouping of the kations is, however, entirely trustworthy. While the difference between the amount of swelling in an acid solution containing a magnesium salt may not differ decidedly from a similar solution made up with a calcium or barium salt, there is never any question about the difference between the action of any of these three and a kation found in the list either above or below them.

(*f*) Non-electrolytes do not share with electrolytes their marked power of reducing through their presence the amount that fibrin will swell in the solution of any alkali or acid. Even when employed in very concentrated solutions, glycerine, urea, saccharose, dextrose, ethyl alcohol, and methyl alcohol do not change the height of the fibrin columns swelling in various concentrations of acid or alkali.

(*g*) The taking up and giving off (absorption and secretion) of water by fibrin represents to a very high degree, a reversible process. If for a hydrochloric acid solution in which fibrin has attained its maximal swelling, an equally concentrated sulphuric acid solution is substituted, the fibrin column shrinks. The

same thing occurs if a potassium hydroxide solution is replaced by an equally concentrated calcium or ammonium hydroxide solution. When equilibrium is finally established the height of the fibrin column in each of these solutions is approximately equal to that which would have been attained had the fibrin been placed directly in these solutions. In the same way fibrin which has attained its maximal swelling in an acid solution will shrink rapidly if for the pure acid there is substituted one of equal concentration containing a salt. Similarly, if water replaces the solution of an acid or an alkali, the fibrin will either shrink or swell more, depending upon whether the addition of the water makes the concentration of the alkali move toward or away from that which is optimal for the swelling of fibrin. (See paragraph *b* of this section.)

The reverse of all these experiments can also be accomplished, although not with the same ease. If, for example, hydrochloric acid is substituted for sulphuric, or potassium hydroxide for the calcium compound, an increase in the amount of swelling is noted, but the column does not rise as high as it would have done if placed directly in these solutions. Similarly, fibrin which has once been in an acid or an alkali solution containing a salt, when placed in pure solutions does not swell to the amount which it would have done if it had been put in these solutions from the first. All this would seem to indicate that fibrin suffers more or less permanently from every external condition to which it has been subjected. To explain this phenomenon we can advantageously call to mind the well-known property of colloids of attaching to themselves, and holding fast the various substances with which they come in contact.

3. Observations on the Swelling of Gelatine.

We have now to consider the important question of whether the behavior of fibrin in various solutions is characteristic of this substance alone, or whether we have simply discussed as applicable

to *one* colloid, properties that are really common to many or to all. A partial answer to our question can be found in the careful studies already available on the swelling of various colloids, particularly gelatine. The observations of Franz Hofmeister,[1] Wolfgang Pauli,[2] K. Spiro,[3] and Wolfgang Ostwald[4] show very clearly that gelatine behaves in many ways entirely similar to fibrin. We will give now a review of some of these observations which are of particular interest to us in the study of our problem. At the same time personal experiments will be introduced which not only serve to corroborate the various findings already made on the swelling of gelatine but augment these, particularly in the following directions. They show (*a*) the unequal effect of different equinormal and equally dissociated acids and alkalies upon the swelling of gelatine; (*b*) the antagonism between neutral salts and acids or alkalies upon the swelling of gelatine; (*c*) the lack of antagonism between non-electrolytes, and acids or alkalies upon the absorption of water by this substance, and (*d*) the reversibility of the absorption of water by this substance.

My own experimental methods differed in no material way from those usually followed by workers in this field. I adopted Ostwald's scheme. The best commercial gelatine (the so-called "Ne Plus Ultra Gelatine" of the Deutsche Gelatine Fabriken) was used. One part of this was dissolved at a low temperature (45° C.) in four parts of water and poured out into shallow pans. After having hardened in an ice-chest the gelatine was cut with the aid of a sharp knife and a ruler into squares of uniform size. These squares were allowed to dry upon glass plates at room temperature. This presented no difficulties, as the room in which I worked for most of the time was very hot (37° C. to 40° C.) and dry. The drying process took from six to ten days, and was not sufficiently rapid to distort the squares. When completely dry the squares measured about 18 x 18 x 2.5 mm. and weighed approximately 0.8 gram. As a uniform material is

[1] Archiv f. exp. Path. u. Pharm. 1890, xxvii, 395; 1891, xxviii, 210.
[2] Pflüger's Archiv, 1897, lxvii, 219; 1898, lxxi, 1.
[3] Beiträge zur chem. Physiologie, 1904, v, 276.
[4] Pflüger's Archiv, 1905, cviii, 563.

necessary to obtain comparable results, it is well to mention that all the gelatine discs used in my experiments were prepared at the same time (June 29, 1908). The course of the absorption of water by the discs was followed by immersing the weighed gelatine discs in solutions of various kinds and weighing them at various intervals.

In order to facilitate comparison with the results obtained on fibrin the paragraphs on gelatine are lettered in the same way as the paragraphs on fibrin. It will be seen that gelatine is a colloid which behaves in many ways like fibrin. Important differences, however, exist between the two, which we shall later find to be not without biological interest.

(*a*) Gelatine swells more in the solution of any acid than it does in water. This fact is readily apparent even to the naked eye. If two gelatine discs are dropped at the same time, the one into water, the other into a $\frac{1}{2}_0$ normal hydrochloric acid solution, the inequality in the amount of swelling is plainly to be seen at the end of six hours, and at the end of twenty-four or forty-eight it is very marked. While at this time the gelatine disc in the water still has a slightly brownish-yellow and opaque appearance, that in the acid is hyaline and perfectly clear, so clear, in fact, that it can scarcely be seen at the bottom of the dish. Spiro, who first discovered this difference in the amount that gelatine will swell in water and in acids, found that while a gelatine plate gained 1.97 times its weight in water, it gained 3.49 times its weight in a $\frac{1}{5}_0$ normal hydrochloric acid solution, and 5.45 times its weight in a $\frac{1}{2}_0$ normal solution. Ostwald came to the same conclusion from comparison of his results on the swelling of gelatine plates in acids of various kinds with the absorption curves of gelatine in water, as given by Hofmeister.

While gelatine swells more in the solution of any acid than in water, the acids are by no means equally potent in this regard when equinormal solutions are compared. While Ostwald considers his experiments too few to permit the expression of a final opinion, he is inclined to the belief that the swelling induced in gelatine discs is exclusively a function of the concentration of the

hydrogen ions in the acid solutions. It seems to me that what has been said for fibrin holds also for gelatine, that the amount of swelling induced is determined by the concentration of the

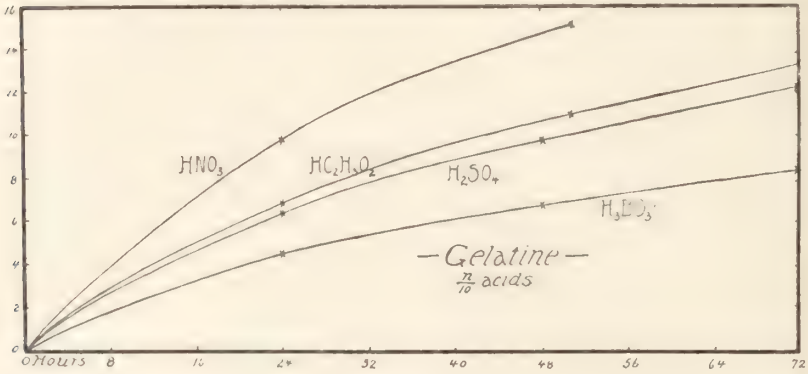


FIGURE 11

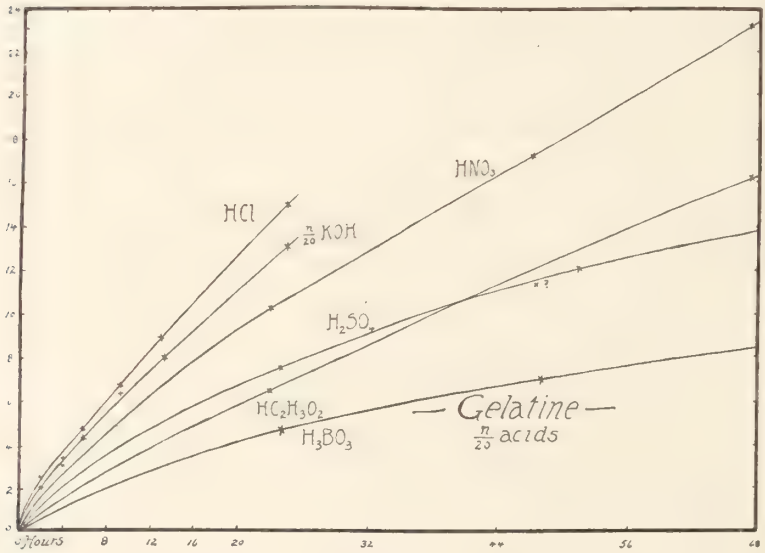


FIGURE 12

hydrogen ions *minus* the effect of the anion of the particular acid concerned. I have taken the liberty of constructing from Ostwald's[1]

[1] Pflüger's Archiv, 1905, cviii, 577 and 578.

tables the curves contained in Figures 11 and 12. The hours that the gelatine discs were in the acid solutions are plotted on the horizontal, the amount of water absorbed, expressed in units of the original weight of the disc, is shown on the vertical. We have no difficulty in recognizing in Figure 11 the order:

Nitric, Acetic, Sulphuric, Boric.

The position of the "weak" acetic acid between the "strong" nitric and sulphuric acids (which two are about equally dissociated, and yield a higher concentration of hydrogen ions than the equinormal acetic acid) is by itself an argument against the explanation which considers *only* the concentration of the hydrogen ions. A look at Figure 12 brings with it similar conclusions. Except in the first hours of the experiment, we again find the order:

Hydrochloric, Nitric, Acetic, Sulphuric, Boric.

This order in which the different acids make gelatine swell is identical with that in which they make fibrin swell.

The amount that gelatine swells in any acid solution is dependent in a complex way upon the concentration of the acid. This is shown in Figure 13, which has been copied from Ostwald's article. The curve marked HCl indicates the amount of water absorbed by gelatine plates after twenty-four hours' residence in hydrochloric acid solutions of various concentrations. With the exception of the initial fall in the curve (which simply indicates that in hydrochloric acid solutions of certain concentrations a gelatine disc may absorb even *less* than in pure water) we notice a rapid rise in the curve indicative of an increase in the amount of swelling with every increase in the concentration of the acid. An optimal point is reached when the concentration of (approximately) a $\frac{1}{3}$'s normal hydrochloric acid is attained, beyond which a further increase in the concentration of the acid is not followed by a greater absorption of water, but by a less.

It will be remembered that an analogous relationship between

concentration of acid and the amount of swelling exists in the case of fibrin.

(*b*) Gelatine swells more in the solution of any alkali than in water. Macroscopic examination alone is sufficient to give

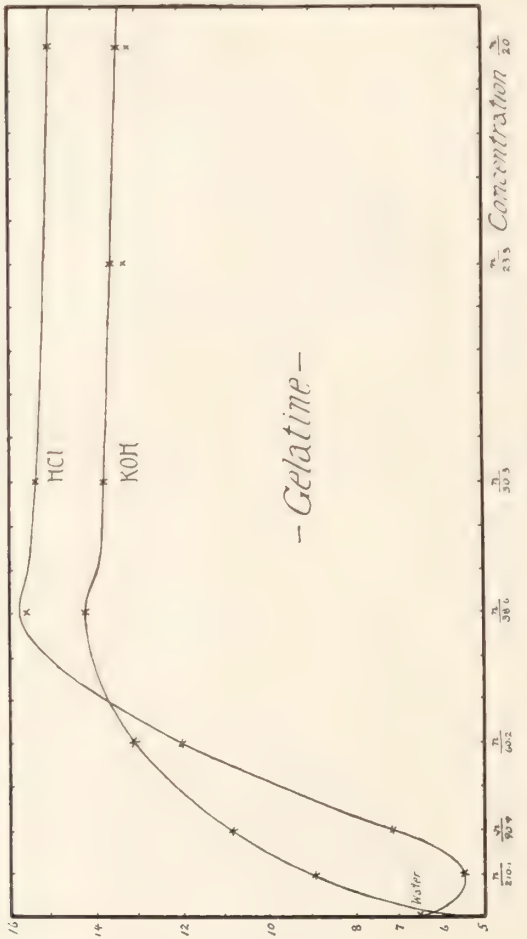


FIGURE 13

evidence of this fact. Spiro,[1] who first showed this to be true, found that while a gelatine disc kept in pure water gained only

[1] Beiträge zur chemischen Physiologie, 1904, v, 277.

3.02 times its weight of water, one kept in a $\frac{1}{100}$ normal sodium hydroxide solution gained 5.08 times its weight, one in a $\frac{1}{50}$ normal solution, 11.82 times its weight, and one in a $\frac{1}{10}$ normal solution, 12.61 times its weight of water.

When the effect of equinormal solutions of different alkalies is compared, it is found that a gelatine disc swells more in some alkalies than in others. This statement which has its analogue

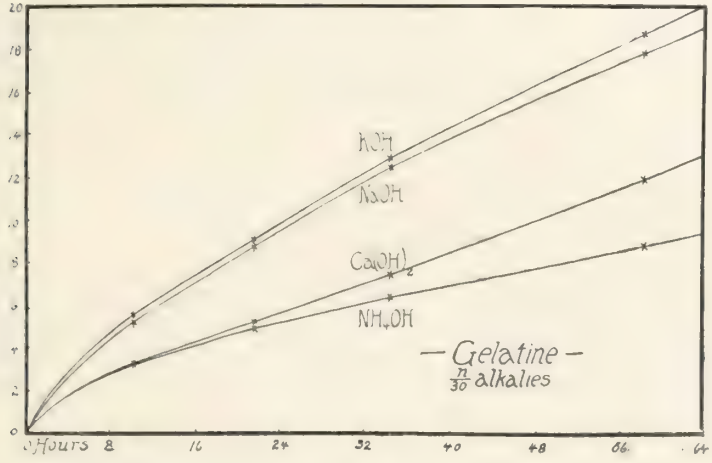


FIGURE 14

in the acids is illustrated in Figure 14. The alkalies show the following grouping, in which that which allows of the greatest swelling is placed first:

Potassium hydroxide,
Sodium hydroxide,
Calcium hydroxide,
Ammonium hydroxide.

At the concentrations employed, the dissociation of the first three of these alkalies is about the same. The conclusion, therefore, seems justified that the swelling of gelatine in various alkalies is determined by the concentration of the hydroxyl ions *minus* the effect of the kation, calcium being more active in bringing

about such a reduction in swelling than sodium, and this more than potassium. Figure 14 has been constructed from the data contained in the following Table B. As the increase in weight in these experiments on gelatine is very considerable, uselessly large figures have been avoided by expressing changes in weight in *parts* of the original weight of the (dry) gelatine. One part, therefore, corresponds to an increase in weight of one hundred per cent.

TABLE B.—*Gelatine.*

Dry weight of gelatine disc.	0.830	0.830	0.830	0.822
Solution.	150 c.c. 1/30 n. KOH.	150 c.c. 1/30 n. NaOH.	150 c.c. 1/30 n. $Ca(OH)_2$	150 c.c. 1/30 n. NH_4OH
Hours in the solution.	Gain in parts of one part of gelatine.			
10.05	5.5	5.3	3.4	3.4
21.25	8.9	8.7	5.2	5.0
34.25	12.8	12.5	7.4	6.8
58.20	18.6	17.7	11.9	8.8

As in the case of hydrochloric acid, so also with potassium hydroxide do we find that the amount of swelling is dependent in a complex way upon the concentration of the alkali. This is well shown in the curve marked KOH in Figure 13, copied from Ostwald. It indicates the amount of water absorbed by gelatine discs after twenty-four hours' residence in various concentrations of potassium hydroxide. The initial rise in the curve indicates how with an increase in the concentration of the alkali there is an increase in the amount of swelling; but, as with the acid, an optimal point is soon reached beyond which a further increase in the concentration of the potassium hydroxide leads to a diminished absorption of water.

(c) If the amounts that gelatine will swell in equinormal solutions of acids and alkalies are compared, it is found that gelatine swells somewhat *less* in the solution of an alkali than in an equally concentrated acid. This fact, which is just the reverse of that found for fibrin, is well illustrated in Figure 13 and in the upper two curves of Figure 12, copied from Ostwald's studies. This observation, it seems to me, finds a ready explanation in the experiments which follow. Commercial gelatine is distinctly

acid in reaction. When this is, therefore, placed in the solution of an alkali, a salt is formed, and, as the next paragraph shows, the presence of any salt markedly decreases the amount that gelatine will swell in any acid or alkaline liquid.

(*d*) The addition of any salt to the solution of an acid or an alkali decreases the amount that a gelatine disc will swell in that solution. As the number of insoluble hydroxides is very large, studies on the antagonism between acids or alkalies and salts were carried out chiefly with acid solutions. Figure 15,

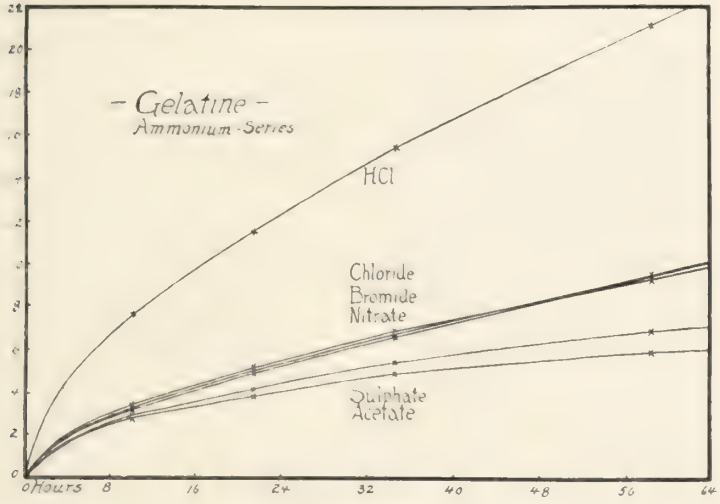


FIGURE 15

as well as Figures 16, 17, 18, 19, 20, 21, and 22, illustrate this point. In Figure 15, there is compared the swelling of a gelatine disc in a pure hydrochloric acid solution, with the swelling of gelatine discs placed in equally concentrated hydrochloric acid solutions to which have been added equimolecular amounts of various ammonium salts. As is clearly evident the amount of swelling is in every instance much less in these solutions than in the pure hydrochloric acid. Figure 15 has been constructed from the data contained in Table C.

TABLE C.—*Gelatine.*

Dry weight of gelatine disc.	0.802	0.806	0.813	0.814	0.817	0.817
Solution.	50 c.c. 1/10 n. HCl + 50 c.c. H_2O	50 c.c. 1/10 n. HCl + 50 c.c. 1/2 m. ammonium acetate.	50 c.c. 1/10 n. HCl + 50 c.c. 1/2 m. ammonium bromide.	50 c.c. 1/10 n. HCl + 50 c.c. 1/2 m. ammonium chloride.	50 c.c. 1/10 n. HCl + 50 c.c. 1/2 m. ammonium nitrate.	50 c.c. 1/10 n. HCl + 50 c.c. 1/2 m. ammonium sulphate.
Hours in the solution.	Gain in parts, of one part of gelatine.					
10.05	7.6	2.8	3.3	3.4	3.2	2.9
21.25	11.4	3.9	5.0	5.2	4.9	4.2
34.25	15.3	4.8	6.7	6.9	6.6	5.3
58.20	21.0	5.8	9.5	9.3	9.5	6.9

The higher the concentration of the added salt, the less does the gelatine swell, and if enough is added the effect of the acid or alkali may be almost entirely suppressed. This fact is brought out in Figures 16, 17, 18, 19, 20, and 21. In each of these figures the curve for the swelling of the gelatine disc is found to lie nearer the base line with every increase in the concentration of salt employed.

(c) When the action of equimolecular salt solutions on the swelling of gelatine discs in acid or alkaline solutions is compared, it is found that some salts depress the amount of swelling more than others. This is already apparent in Figure 15, in which the sulphate and acetate of ammonium have brought about a distinctly greater inhibition in swelling than the chloride, bromide, and nitrate. The point is further illustrated by comparing with each other Figures 16, 17, and 18; also Figures 19, 20, and 21. The hydrochloric acid curves of Figures 16, 17, and 18 are practically identical. In all the figures a diminution in the amount of swelling is apparent through the addition of the salts, and the more salt added, the greater is this diminution. When Figure 16 is compared with Figure 17, it is readily apparent that at the same concentration, potassium citrate brings about a greater depression of swelling in an acid solution than potassium chloride. When, now, we compare Figure 18 with Figure 16, we note that potassium sulphocyanate acts more powerfully than potassium chloride. The relations are not as simple, however, in the case of gelatine as in the case of fibrin, for when we compare Figure 17 with Figure 18, we find that the extremes of the potassium

citrate series lie between the extremes of the potassium sulphocyanate series. We cannot, in consequence, make out even a short table to indicate the order in which various *anions* are

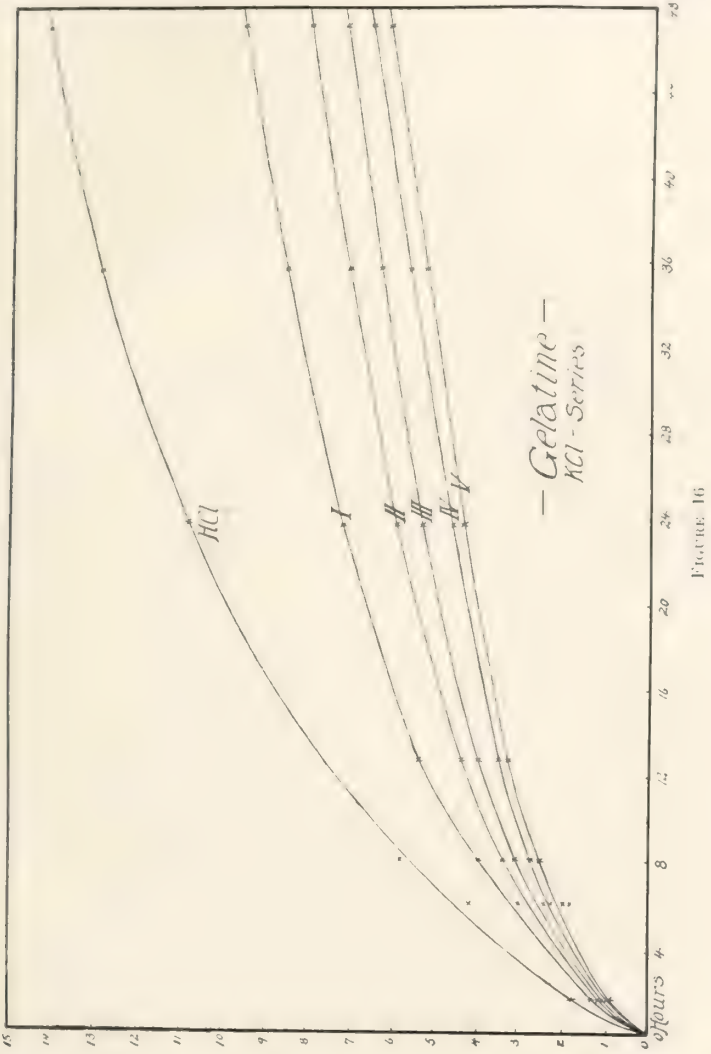


FIGURE 16

active in depressing the amount that gelatine will swell in an acid solution without stating the exact concentrations of salt used.

Figures 19, 20, and 21, permit a comparison of various *kations*.

When Figures 19 and 20 are compared, it is readily apparent that calcium chloride is more effective in inhibiting the swelling

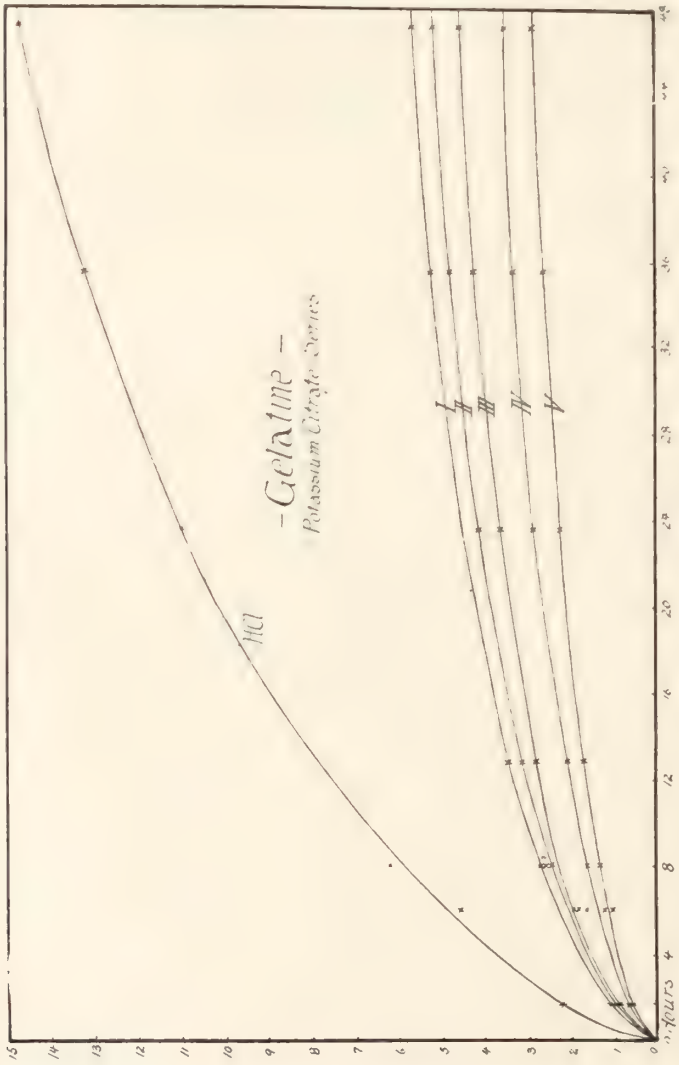


FIGURE 17

of gelatine in an acid solution than is potassium chloride. All the curves of Figure 20 (with the exception of the pure hydrochloric acid curves, which almost coincide) lie distinctly below

the corresponding curves in Figure 19.[1] If we make a little allowance for experimental errors we are probably safe in saying

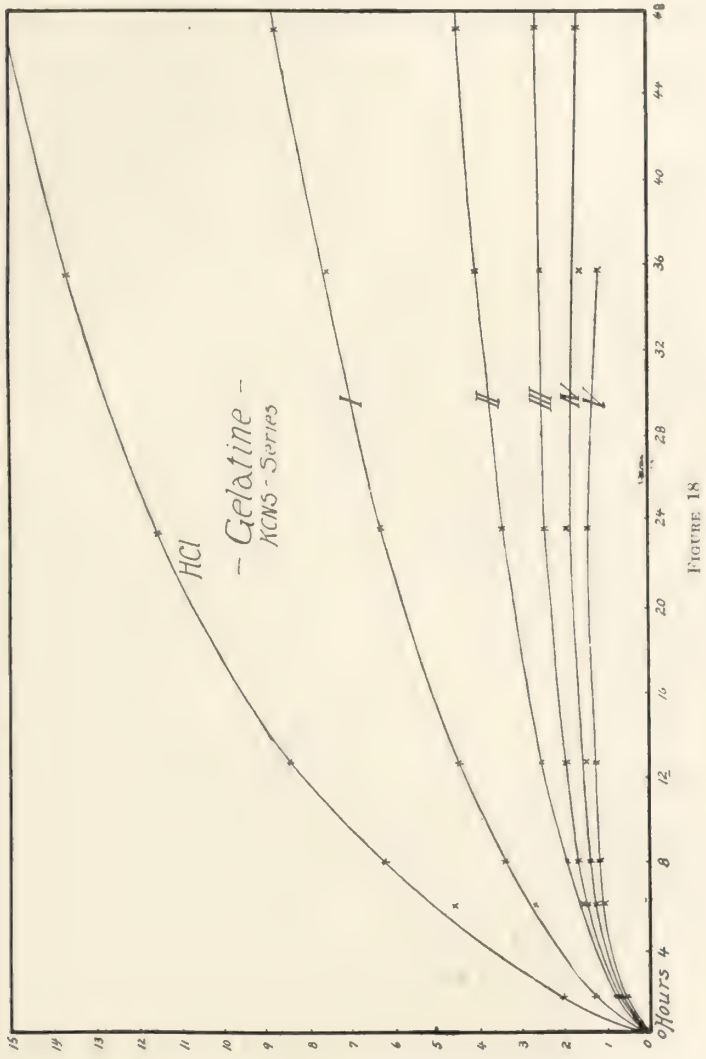


FIGURE 18

[1] That curve V in Figure 20 lies above IV is simply due to the fact that the dry gel tine disc used for curve V was not as heavy as that used for curve IV. Thin discs sw not only faster but somewhat more than thicker ones.

that the curves for sodium chloride in Figure 21 occupy a position between those given for potassium chloride and calcium chloride.

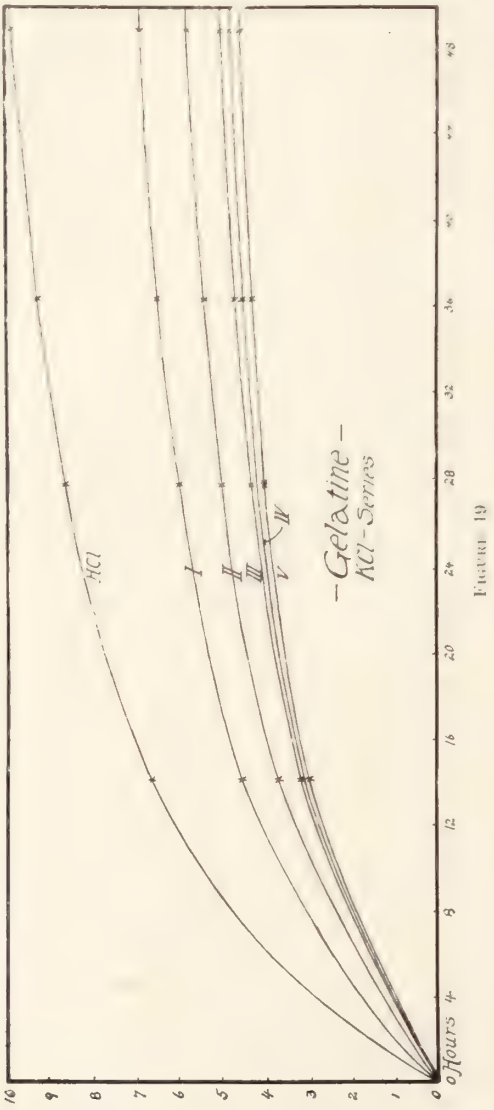


FIGURE 19

As the anion is the same in these salts, these differences may be attributed to the effect of the kations which assume the following

familiar order in which the ion least effective in reducing the swelling of gelatine is placed first.

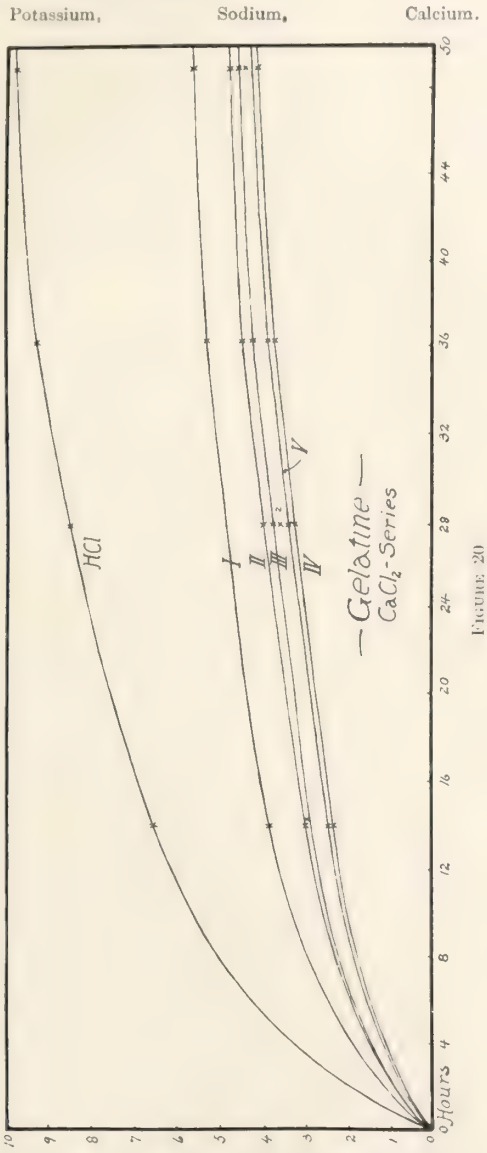


FIGURE 20

As the concentrations of acids and salts employed are the same in the experiments from which Figures 16 and 19 (the two

potassium chloride series) have been constructed, the question of why the curves in the latter lie so much lower than those in

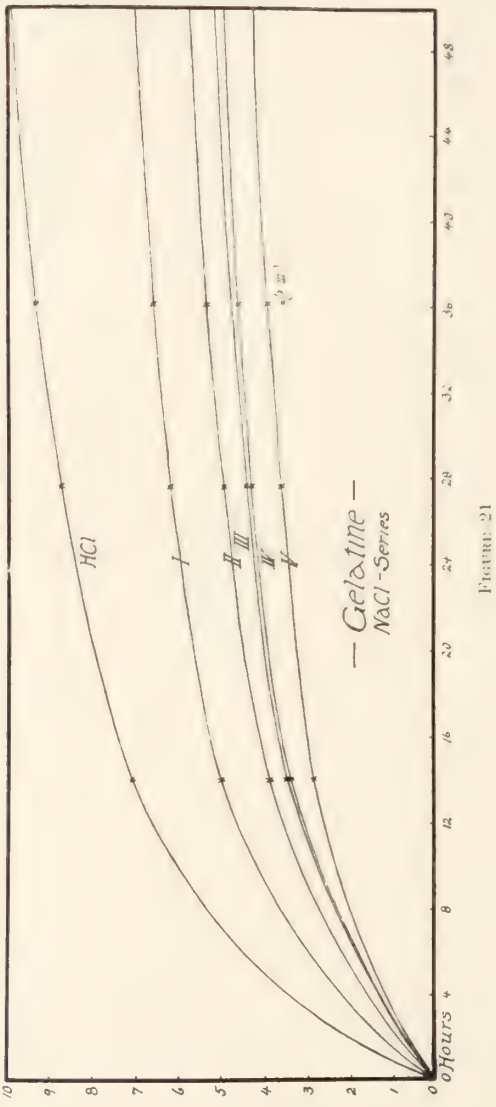


FIGURE 21

the former arises. All external conditions were the same in these two sets of experiments except the temperature, and it is

to the higher temperature prevailing when the experiments of Figures 16, 17, and 18 were carried out (September 4 to 7, 1908) than when those of Figures 19, 20, and 21 were made (November 11 to 20, 1908), that I attribute the marked absolute differences in the amount of the swelling.

Another point of interest in connection with Figures 16 to 21 is the amount of inhibition in the swelling with any unit increase in the concentration of the added salt. *It is clearly evident that*

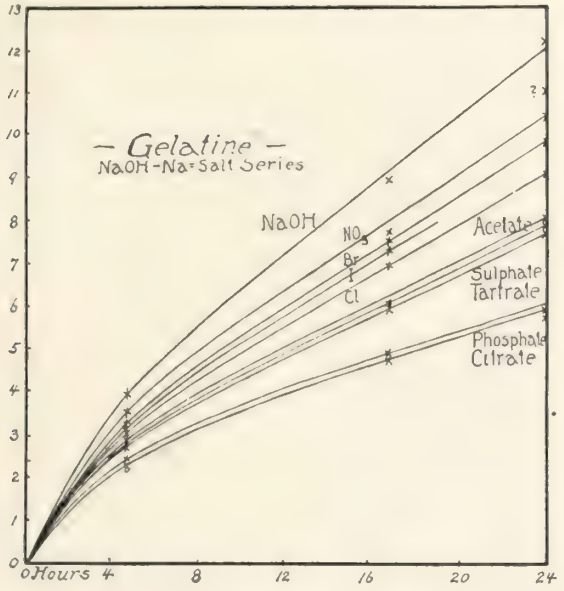


FIGURE 22

to double the concentration of the salt is not to double the diminution in swelling—in every case the diminution is less than might be expected. This is a fact not without biological significance, and one to which we will want to return.

In Figure 22 is illustrated the effect of adding equimolecular solutions of different sodium salts to a solution of sodium hydroxide. It is easily seen how much more powerfully the citrate, phosphate, tartrate, and sulphate interfere with the swelling of the gelatine discs in this alkaline solution, than the various univalent ions.

The general grouping of ions as to the way in which they affect the swelling of gelatine in solutions of acids and alkalies is therefore the same as that discovered in our study of the swelling of fibrin.

The succeeding Tables D, E, F, G, H, I, J contain the experimental data from which have been constructed, respectively, Figures 16, 17, 18, 19, 20, 21, and 22.

TABLE D.—*Gelatine.*

Dry weight of gelatine disc.	0.800	0.802	0.803	0.809	0.810	0.813
Solution.	50 c.c. 1/10 n. HCl + 40 c.c. H_2O + 10 c.c. 1/1 m. potassium chloride.	50 c.c. 1/10 n. HCl + 30 c.c. H_2O + 20 c.c. 1/1 m. potassium chloride.	50 c.c. 1/10 n. HCl + 20 c.c. H_2O + 30 c.c. 1/1 m. potassium chloride.	50 c.c. 1/10 n. HCl + 10 c.c. H_2O + 40 c.c. 1/1 m. potassium chloride.	50 c.c. 1/10 n. HCl + 50 c.c. 1/1 m. potassium chloride.	50 c.c. 1/10 n. HCl + 50 c.c. H_2O.
Hours in the solution.	Gain in parts, of one part of gelatine.					
1.40	1.36	1.21	1.21	1.03	1.00	1.81
6.05	3.02	2.49	2.39	2.05	1.87	4.26
8.05	4.11	3.42	3.17	2.75	2.53	5.86
12.40	5.41	4.48	4.06	3.57	3.32	6.63
23.35	7.27	6.01	5.40	4.66	4.48	10.82
35.25	8.56	7.06	6.34	5.67	5.29	12.79
47.05	9.58	8.01	7.21	6.51	6.11	14.16
	I	II	III	IV	V	

TABLE E.—*Gelatine.*

Dry weight of gelatine disc.	0.763	0.765	0.766	0.772	0.775	0.778
Solution.	50 c.c. 1/10 n. HCl + 40 c.c. H_2O + 10 c.c. 1/1 m. potassium citrate.	50 c.c. 1/10 n. HCl + 30 c.c. H_2O + 20 c.c. 1/1 m. potassium citrate.	50 c.c. 1/10 n. HCl + 20 c.c. H_2O + 30 c.c. 1/1 m. potassium citrate.	50 c.c. 1/10 n. HCl + 10 c.c. H_2O + 40 c.c. 1/1 m. potassium citrate.	50 c.c. 1/10 n. HCl + 50 c.c. 1/1 m. potassium citrate.	50 c.c. 1/10 n. HCl + 50 c.c. H_2O.
Hours in the solution.	Gain in parts, of one part of gelatine.					
1.40	1.11	1.01	0.95	0.73	0.61	2.20
6.05	1.93	1.86	1.68	1.25	1.02	4.55
8.05	2.64	2.46	2.61 (?)	1.64	1.33	6.22
12.40	3.39	3.13	2.81	2.08	1.65	6.93
23.35	4.42	4.04	3.63	2.80	2.21	11.13
35.25	5.12	4.67	4.15	3.26	2.56	13.13
47.05	5.57	5.09	4.52	3.59	2.84	14.61
	I	II	III	IV	V	

TABLE F.—*Gelatine.*

Dry weight of gelatine disc.	0.778	0.782	0.783	0.788	0.790	0.794
Solution.	50 c.c. 1/10 n. HCl + 40 c.c. H_2O + 10 c.c. 1/1 m. potassium sulpho-cyanate.	50 c.c. 1/10 n. HCl + 30 c.c. H_2O + 20 c.c. 1/1 m. potassium sulpho-cyanate.	50 c.c. 1/10 n. HCl + 20 c.c. H_2O + 30 c.c. 1/1 m. potassium sulpho-cyanate.	50 c.c. 1/10 n. HCl + 10 c.c. H_2O + 40 c.c. 1/1 m. potassium sulpho-cyanate.	50 c.c. 1/10 n. HCl + 50 c.c. 1/1 m. potassium sulpho-cyanate.	50 c.c. 1/10 n. HCl + 50 c.c. H_2O.
Hours in the solution.	Gain in parts, of one part of gelatine.					
1.40	1.33	0.86	0.82	0.73	0.68	2.06
6.05	2.68	1.54	1.40	1.25	1.07	4.61
8.05	3.46	1.96	1.65	1.32	1.16	6.27
12.40	4.47	2.54	1.93	1.47	1.18	8.43
23.35	6.28	3.36	2.42	1.85	1.43	11.49
35.25	7.50	3.93	2.56	1.56	1.11	13.58
47.05	8.74	4.56	2.66	1.56	Too sticky to weigh	15.07
	I	II	III	IV	V	

TABLE G.—*Gelatine.*

Dry weight of gelatine disc.	0.755	0.792	0.755	0.771	0.722	0.750
Solution.	50 c.c. 1/10 n. HCl + 40 c.c. H_2O + 10 c.c. 1/1 m. potassium chloride.	50 c.c. 1/10 n. HCl + 30 c.c. H_2O + 20 c.c. 1/1 m. potassium chloride.	50 c.c. 1/10 n. HCl + 20 c.c. H_2O + 30 c.c. 1/1 m. potassium chloride.	50 c.c. 1/10 n. HCl + 10 c.c. H_2O + 40 c.c. 1/1 m. potassium chloride.	50 c.c. 1/10 n. HCl + 50 c.c. 1/1 m. potassium chloride.	50 c.c. 1/10 n HCl + 50 c.c. H_2O.
Hours in the solution.	Gain in parts, of one part of gelatine.					
14.00	4.5	3.7	3.2	3.2	3.0	6.5
27.35	5.9	4.9	4.2	4.0	3.8	8.6
36.15	6.4	5.3	4.6	4.5	4.2	9.2
48.45	6.8	5.8	5.0	4.8	4.6	9.8
75.35	7.5	6.3	5.8	5.6	5.3	11.0
144.15	9.2	7.9	7.0	6.9	6.4	12.9
213.15	10.3	8.9	7.8	7.7	7.2	14.4
	I	II	III	IV	V	

TABLE H.—*Gelatine.*

Dry weight of gelatine disc.	0.724	0.743	0.723	0.788	0.738	0.740
Solution.	50 c.c. 1/10 n. HCl + 40 c.c. H_2O + 10 c.c. 1/1 m. calcium chloride.	50 c.c. 1/10 n. HCl + 30 c.c. H_2O + 20 c.c. 1/1 m. calcium chloride.	50 c.c. 1/10 n. HCl + 20 c.c. H_2O + 30 c.c. 1/1 m. calcium chloride.	50 c.c. 1/10 n. HCl + 10 c.c. H_2O + 40 c.c. 1/1 m. calcium chloride.	50 c.c. 1/10 n. HCl + 50 c.c. 1/1 m. calcium chloride.	50 c.c. 1/10 n. HCl + 50 c.c. H_2O.
Hours in the solution.	Gain in parts, of one part of gelatine.					
14.00	3.8	2.9	2.9	2.3	2.4	6.5
27.35	3.5	3.9	3.7	3.2	3.4	8.4
36.15	5.3	4.4	4.2	3.7	3.9	9.2
48.45	5.6	4.7	4.6	4.1	4.4	9.7
75.35	6.4	5.5	5.4	5.0	5.4	10.9
144.15	7.6	6.8	6.8	6.8	7.4	12.9
213.15	8.5	7.6	7.8	7.9	8.7	14.6
	I	II	III	IV	V	

TABLE I.—*Gelatine.*

Dry weight of gelatine disc.	0.632	0.690	0.686	0.597	0.700	0.676
Solution.	50 c.c. 1/10 n. HCl + 40 c.c. H_2O + 10 c.c. 1/1 m. sodium chloride.	50 c.c. 1/10 n. HCl + 30 c.c. H_2O + 20 c.c. 1/1 m. sodium chloride.	50 c.c. 1/10 n. HCl + 20 c.c. H_2O + 30 c.c. 1/1 m. sodium chloride.	50 c.c. 1/10 n. HCl + 10 c.c. H_2O + 40 c.c. 1/1 m. sodium chloride.	50 c.c. 1/10 n. HCl + 50 c.c. 1/1 m. sodium chloride.	50 c.c. 1/10 n. HCl + 50 c.c. H_2O.
Hours in the solution.	Gain in parts, of one part of gelatine.					
14.00	5.0	3.9	3.5	3.5	2.8	7.1
27.35	6.2	4.9	4.4	4.3	3.6	8.7
36.15	6.6	5.3	3.5 (?)	4.6	3.9	9.3
48.45	7.0	5.7	5.1	4.9	4.2	9.8
75.35	7.8	6.3	5.6	5.4	4.8	10.8
144.15	9.1	7.6	6.9	6.5	5.9	12.7
213.15	10.0	8.4	7.5	6.9	6.6	14.2
	I	II	III	IV	V	

TABLE J.—*Gelatine.*

Dry weight of gelatine disc.	0.799	0.798	0.797	0.787	0.782
Solution.	50 c.c. 1/10 n. NaOH + 50 c.c. H_2O.	50 cc. 1/10 n. NaOH + 50 c.c. 1/5 m. sodium acetate.	50 c.c. 1/10 n. NaOH + 50 c.c. 1/5 m. sodium bromide.	50 c.c. 1/10 n. NaOH + 50 c.c. 1/5 m. sodium chloride.	50 c.c. 1/10 n. NaOH + 50 c.c. 1/5 m. sodium citrate.
Hours in the solution.	Gain in parts, of one part of gelatine.				
4.45	3.94	2.71	3.37	3.14	2.22
17.00	8.83	6.00	7.42	6.91	4.73
24.30	12.38	8.12	9.83	9.29	6.23
47.30	melted	too soft to weigh	too soft to weigh	too soft to weigh	8.65 much broken

Dry weight of gelatine disc.	0.776	0.770	0.756	0.755	0.754
Solution.	50 c.c. 1/10 n. NaOH + 50 c.c. 1/5 m. sodium iodide.	50 c.c. 1/10 n. NaOH + 50 c.c. 1/5 m. sodium nitrate.	50 c.c. 1/10 n. NaOH + 50 c.c. 1/5 m. disodium phosphate.	50 c.c. 1/10 n. NaOH + 50 c.c. 1/5 m. sodium sulphate.	50 c.c. 1/10 n. NaOH + 50 c.c. 1/5 m. NaK tartrate.
Hours in the solution.	Gain in parts, of one part of gelatine.				
4.45	3.34	3.46	2.41	2.95	2.88
17.00	7.40	7.58	4.78	6.04	5.95
24.30	11.02	10.40	6.10	8.08	7.82
47.30	melted	almost melted	9.11 good body	breaks on handling	firmer than preceding

f) Non-electrolytes do not share with electrolytes their marked power of reducing through their presence the amount that gelatine will swell in the solution of any acid or alkali. Figures 23, 24, and 25 illustrate this fact better than words. The upper curve of Figure 23 indicates the amount and rate of swelling of a gelatine disc in a pure hydrochloric acid solution. The *black* circles, crosses, squares, and triangles just below this curve give the gains in weight of gelatine discs kept in equally concentrated hydrochloric acid solutions to which various amounts of *ethyl alcohol* have been added. While present in amounts *osmotically* more than equivalent to the salts added in the previously described experiments, there is practically no reduction in the amount of the swelling of the gelatine discs. The same is found to be true when *methyl alcohol* is added to a hydrochloric acid solution. To avoid confusion only one of these curves has been drawn in,

and the whole series has been placed somewhat to the right in the drawing. The methyl alcohol series is indicated in *white* crosses, squares, circles, and triangles to distinguish it from the

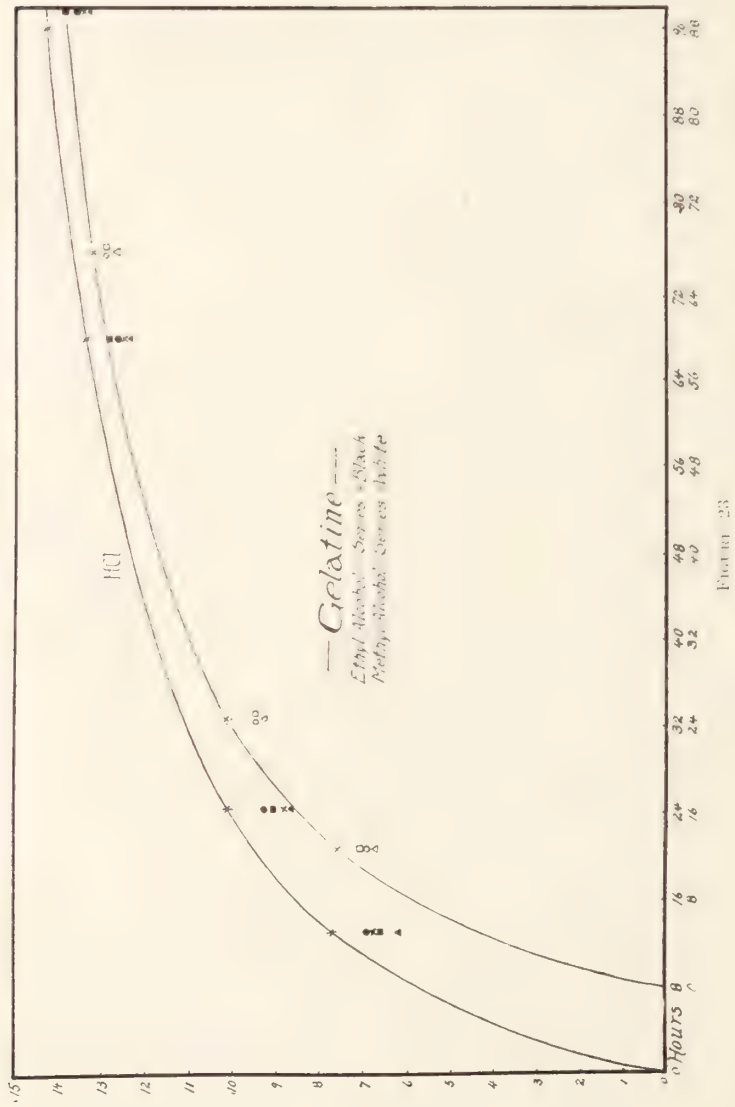


FIGURE 23

ethyl alcohol series. As is readily apparent, these characters practically coincide with each other.

In Figure 24 is shown the effect of adding various amounts

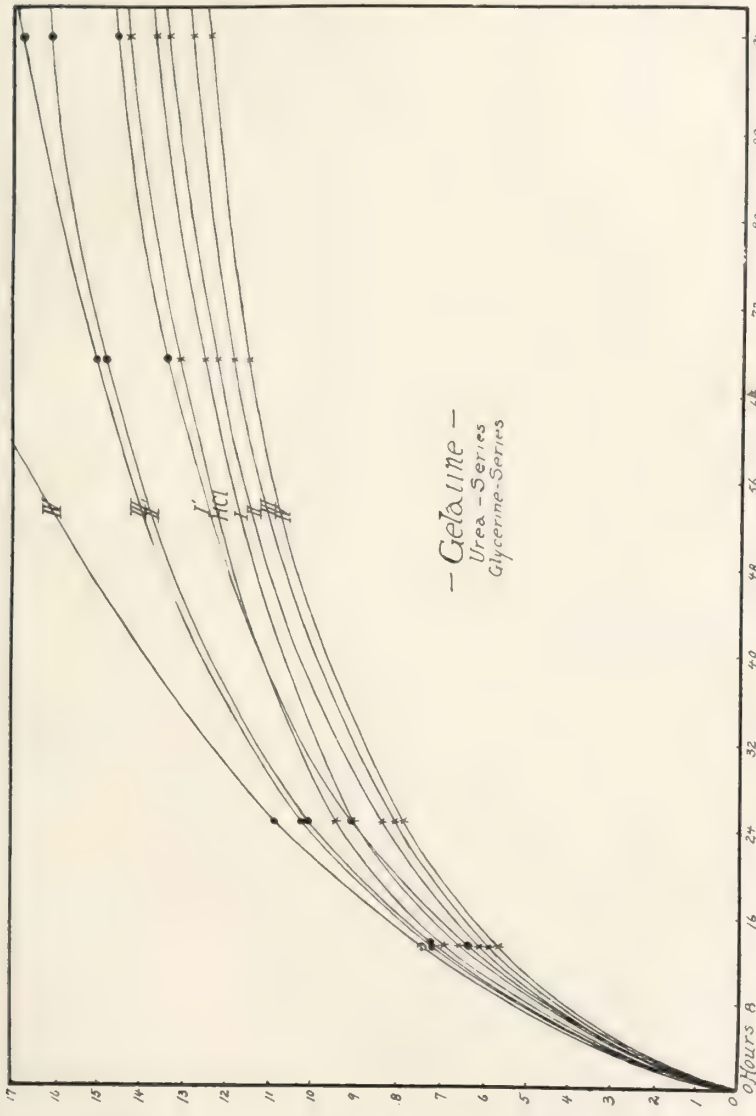


FIGURE 24

of *glycerine* and *urea* to a hydrochloric acid solution. The curve for the pure hydrochloric acid solution occupies a position at about the middle of the series. The curves marked I, II, III, and IV show the effect on swelling of adding progressively larger amounts of *glycerine* to the hydrochloric acid solution. Glycerine produces a definite decrease in the amount of swelling, though

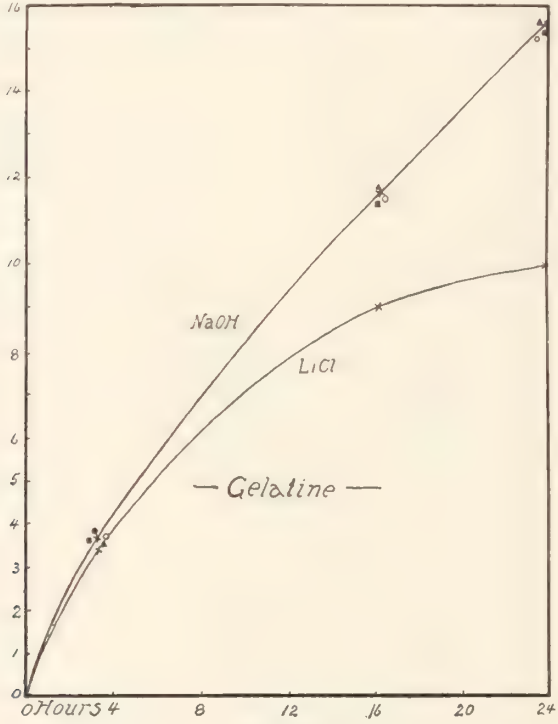


FIGURE 25

as compared with the effect of any electrolyte, this is very slight. *Urea*, on the other hand, distinctly *favors* the swelling of gelatine in a hydrochloric acid solution, and this the more, the higher the concentration of the urea. The curves marked I′, II′, III′, and IV′ demonstrate this fact very clearly.

The effect of various non-electrolytes on the swelling of gelatine in an alkaline solution is shown in Figure 25. As in the case

with acids, urea again seems to favor the swelling of the gelatine. The addition of ethyl and methyl alcohols and glycerine is without effect, for these curves practically coincide with that for the pure alkali. In contrast hereto the addition of an electrolyte, lithium chloride, produces a distinct diminution in the amount of the swelling.

The curves of Figures 23, 24, and 25 have been constructed from the experimental data contained in Tables K, L, and M respectively.

TABLE K.—*Gelatine.*

Dry weight of gelatine disc.	0.773	0.765	0.756	0.748	0.723
Solution.	50 c.c. 1/10 n. HCl + 40 c.c. H_2O + 10 c.c. 2/1 m. ethyl alcohol.	50 c.c. 1/10 n. HCl + 30 c.c. H_2O + 20 c.c. 2/1 m. ethyl alcohol.	50 c.c. 1/10 n. HCl + 20 c.c. H_2O + 30 c.c. 2/1 m. ethyl alcohol.	50 c.c. 1/10 n. HCl + 50 c.c. 2/1 m. ethyl alcohol.	50 c.c. 1/10 n. HCl + 50 c.c. H_2O.
Hours in the solution.	Gain in parts, of one part of gelatine.				
13.20	6.9	6.7	6.8	6.2	7.7
24.45	9.2	9.1	8.8	8.7	10.1
67.30	12.5	12.7	12.4	12.3	13.2
97.05	13.5	13.8	13.5	13.4	14.2
113.35	13.8	14.1	13.9	13.9	14.6
162.45	14.4	14.7	14.5	14.4	15.1
212.05	14.7	15.0	14.8	14.7	15.5
13 days	15.4	15.6	15.3	15.0	16.2
	Circle	Square	Cross	Triangle	
	Black				

Dry weight of gelatine disc.	0.733	0.729	0.727	0.724
Solution.	50 c.c. 1/10 n. HCl + 40 c.c. H_2O + 10 c.c. 2/1 m. methyl alcohol.	50 c.c. 1/10 n. HCl + 30 c.c. H_2O + 20 c.c. 2/1 m. methyl alcohol.	50 c.c. 1/10 n. HCl + 20 c.c. H_2O + 30 c.c. 2/1 m. methyl alcohol.	50 c.c. 1/10 n. HCl + 50 c.c. 2/1 m. methyl alcohol.
Hours in the solution.	Gain in parts, of one part of gelatine.			
13.20	7.6	6.9	7.1	6.7
24.45	10.1	9.4	9.4	9.2
67.30	13.1	12.7	12.7	12.5
97.05	14.0	13.7	13.7	13.5
113.35	14.4	13.9	14.1	13.9
162.45	14.9	14.6	14.6	14.3
212.05	15.4	14.9	14.9	14.1
13 days	16.0	15.5	15.4	15.2
	Star	Circle	Square	Triangle
	White			

TABLE L.—*Gelatine.*

Dry weight of gelatine disc.	0.829	0.872	0.842	0.816	0.810
Solution.	50 c.c. 1/10 n. HCl + 40 c.c. H_2O + 10 c.c. 2/1 m. glycerine.	50 c.c. 10 n. HCl + 30 c.c. H_2O + 20 c.c. 2/1 m. glycerine.	50 c.c. 1/10 n. HCl + 20 c.c. H_2O + 30 c.c. 2/1 m. glycerine.	50 c.c. 1/10 n. HCl + 50 c.c. 2/1 m. glycerine.	50 c.c. 1/10 n. HCl + 50 c.c. H_2O.
Hours in the solution.	Gain in parts, of one part of gelatine.				
13.20	6.6	6.1	5.9	5.6	6.9
24.45	9.0	8.2	8.1	7.8	9.4
67.30	12.5	12.2	11.7	11.4	13.1
97.05	13.6	13.3	12.8	12.4	14.2
113.35	13.9	13.7	13.1	12.7	14.6
162.45	14.5	14.3	13.7	13.2	15.2
212.05	14.8	14.6	14.0	13.5	15.6
13 days	15.3	15.1	14.5	14.0	17.0
	I	II	III	IV	

Dry weight of gelatine disc.	0.851	0.848	0.837	0.832
Solution.	50 c.c. 1/10 n. HCl + 40 c.c. H_2O + 10 c.c. 2/1 m. urea.	50 c.c. 1/10 n. HCl + 30 c.c. H_2O + 20 c.c. 2/1 m. urea.	50 c.c. 1/10 n. HCl + 20 c.c. H_2O + 30 c.c. 2/1 m. urea.	50 c.c. 1.10 n. HCl + 50 c.c. 2/1 m. urea.
Hours in the solution.	Gain in parts, of one part of gelatine.			
13.20	6.4	7.2	7.2	7.3
24.45	9.1	10.1	10.2	10.8
67.30	13.3	14.7	15.0	18.1
97.05	14.5	16.1	16.7	20.7
113.35	15.1	16.6	17.3	21.5
162.45	15.7	17.4	18.4	23.1
212.05	16.0	17.7	18.8	23.7
13 days	16.8	18.6	19.5	24.5
	I′	II′	III′	IV′

TABLE M.—*Gelatine.*

Dry weight of gelatine disc.	0.710	0.712	0.714	0.715	0.716	0.705
Solution.	50 c.c. 1/10 n. NaOH + 50 c.c. 1.5 m. LiCl.	50 c.c. 1/10 n. NaOH + 50 c.c. 2/5 m. urea.	50 c.c. 1/10 n. NaOH + 50 c.c. 2/5 m. glycerine.	50 c.c. 1/10 n. NaOH + 50 c.c. 2/5 m. ethyl alcohol.	50 c.c. 1/10 n. NaOH + 50 c.c. 2/5 m. methyl alcohol.	50 c.c. 1/10 n. NaOH + 50 c.c. H_2O.
Hours in the solution.	Gain in parts, of one part of gelatine.					
3.15	3.46	3.70	3.71	3.70	3.64	3.80
16.15	9.07	12.45	11.53	11.79	11.51	11.70
24.00	9.98	13.57	15.79	15.29	15.60	15.82
		Melting Black circle	White circle	Triangle	Square	

(g) The absorption and secretion of water by gelatine represent in large part reversible processes. This fact is brought out in Figure 26 and Table N, from which it is constructed. When a gelatine disc is transferred from a pure hydrochloric acid or sodium hydroxide solution into an equally concentrated one

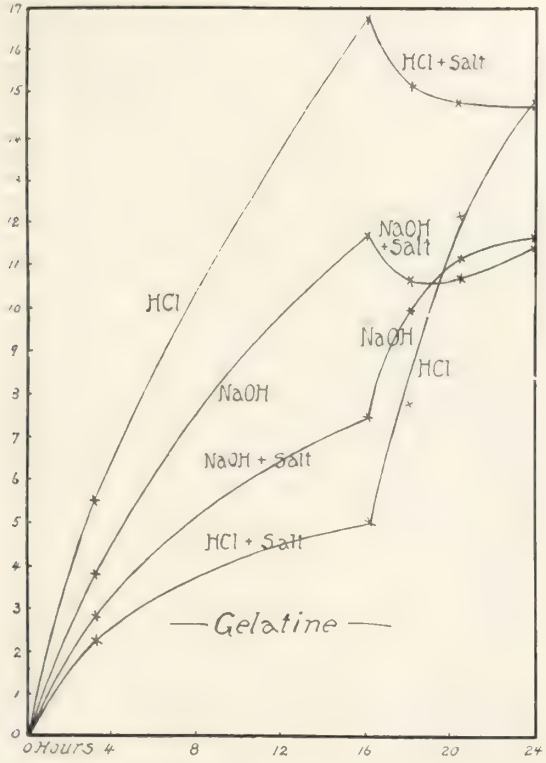


FIGURE 26

containing a salt, a prompt fall in the absorption curve is noted. A rise in the curve follows the reverse process. A further fact of interest in Figure 26 is that at the same concentration potassium citrate inhibits the swelling of gelatine in a hydrochloric acid solution more than in an equinormal sodium hydroxide solution.

TABLE N.—*Gelatine.*

Dry weight of gelatine disc.	I 0.705	II 0.705	III 0.722	IV 0.721
Solution.	50 c.c. 1/10 n. NaOH + 50 c.c. H_2O.	50 c.c. 1/10 n. NaOH + 50 c.c. 1/5 m. K citrate.	50 c.c. 1/10 n. HCl + 50 c.c. H_2O.	50 c.c. 1/10 n. HCl + 50 c.c. 1/5 m. K citrate.
Hours in the solution.	Gain in parts, of one part of gelatine.			
3.15	3.80	2.74	5.44	2.26
16.15	11.70	7.39	16.74	5.02
	Disc I is put into Solution II; Disc II into Solution I. Disc III is put into Solution IV; Disc IV into Solution III.			
18.25	10.49	9.85	15.20	7.64
20.35	10.63	11.19	14.70	12.26
24.00	11.21	11.34	14.72	14.77

It is well in concluding this section to say a word regarding the *similarities and the differences to be noted between the swelling of fibrin and the swelling of gelatine.* The two behave similarly in that both swell more in the solutions of acids and alkalies than in water; both swell to different degrees in equinormal solutions of different acids or alkalies, and the order in which these acids and alkalies are effective is much the same; the swelling of both in either acid or alkaline solutions is markedly inhibited through the presence of electrolytes, and this the more, the higher the concentration of the electrolytes. In contrast to the action of the electrolytes, the non-electrolytes are comparatively ineffective in this regard.

There exist, on the other hand, certain differences between the swelling of fibrin and the swelling of gelatine. These are for the most part of a quantitative nature. Thus the absolute amount of water that may be taken up by fibrin seems to be much greater than that which can be taken up by gelatine. Gelatine is able to absorb under the best conditions about twenty-five times its weight of water. With fibrin I have obtained values as high as forty times its weight in absorbed water. While fibrin swells more in alkaline solutions than in equally concentrated acid solutions, gelatine does just the reverse. This may, however, be only a seeming difference, because of the usual acid reaction of the commercial gelatines, and the consequent forma-

tion of salts when these are made to swell in alkaline solutions. Fibrin attains its maximal swelling in concentrations of acid which are much below those necessary to produce the maximum amount of swelling in gelatine, and much higher concentrations of electrolytes are necessary to markedly reduce the swelling of gelatine in acid solutions than are necessary in the case of fibrin.

From a qualitative standpoint it is noteworthy that the swelling of gelatine in an acid solution is favored by urea, while no such effect is evident with fibrin. The salts, also, which behave in a very simple way toward fibrin, allowing of their ready classification, do not seem to behave quite so simply when gelatine is employed. Finally, neutral gelatine swells to very different amounts in salt solutions of various kinds, while fibrin, to all intents and purposes, swells no more in one salt solution than in another, if an acid or an alkali is not simultaneously present.

These differences and similarities in the behavior of different colloids toward the same external conditions demand detailed study, for they are of the utmost biological importance. Protoplasm consists, as is well known, of a mixture of many different colloids. Not only are different colloids found in the same cell, but essentially different colloids form the basis of different tissues (bone, cartilage, muscle, connective tissue, parenchymatous organs, central nervous system). It is at once apparent, therefore, that not only so far as water absorption and secretion is concerned, but so far as any physiological reaction dependent upon the colloidal constitution of living matter is concerned, a single variation in internal or external conditions may be followed by quite a different response either qualitatively or quantitatively, not only by different tissues but by different parts of the same tissue or even the same cell. In a study of the behavior of different colloids toward the same group of external conditions we may therefore hope to discover much to aid us in our attempt to analyze the apparently limitless variations in the reactions of protoplasm to various external "stimuli."

IV. THE ANALOGY BETWEEN THE SWELLING OF CERTAIN COLLOIDS AND THE SWELLING OF PROTOPLASM.

Having become familiar with the effect of various external conditions on the swelling of two simple so-called hydrophilic or emulsion colloids (fibrin and gelatine), we have now at our disposal some facts which we may utilize in an attempt to analyze the ways and means by which tissues hold their normal amount of water, and to discover how under altered external conditions they may come to hold more or less that is considered normal. It is clearly evident that could we show that the same conditions which make fibrin or gelatine take up and give off water affect protoplasm similarly, a real step forward in the solution of this problem of the absorption and secretion of water by the tissues would be made. This can be done and with great simplicity. As the following paragraphs show, *the absorption of water by muscle or the absorption of water by the eyeball is entirely analogous to the absorption of water by fibrin or by gelatine.*

1. The Analogy between the Absorption of Water by Fibrin and by Muscle.

Simple facts regarding the absorption of water by muscle are very numerous and date back to the earliest periods of modern physiology. For our purposes it is useless to review those which antedate the years in which adequate use of the principles of physical chemistry first began to be made in biological studies. The period of interest to us begins with 1898, when Jacques Loeb[1] published the results of some experiments on the influence of acids, alkalies, and various salts on the absorption of water by the gastrocnemius muscle of the frog. He found that muscle

[1] Pflüger's Archiv f. d. ges. Physiologie, 1898, lxix, 1; ibid., 1898, lxxi, 457; ibid., 1899, lxxv, 303.

absorbs much water if placed in distilled water or in solutions of various acids and alkalies. From his earlier experiments he concluded that a muscle does not change in weight if kept in a solution having an osmotic pressure equal to that of the blood, but that it gains or loses weight if placed in solutions having respectively a lower or a higher osmotic pressure. This later statement was subsequently modified when he discovered that in spite of isosmoticity a frog's muscle will absorb more water from a potassium chloride solution than from one of sodium chloride, and more from this than from one of calcium chloride. The analogy between the latter fact and the absorption of water by potassium, sodium, and calcium soaps was pointed out, but our conceptions of the colloids had not at that time advanced to the point of recognizing in the soaps examples of this class of bodies. The action of acids and alkalies on muscle, Loeb brought into harmony with his osmotic conceptions of absorption by assuming that the hydrogen and hydroxyl ions brought about hydrolytic cleavages within the muscle tissues whereby the osmotic pressure of the cell contents was raised.

The experiments of Ralph W. Webster[1] and E. Overton[2] followed those of Loeb. Webster concluded that osmotic effects could only explain the absorption from water and solutions of cane sugar. His careful study of the effects of electrolytes showed unequivocally that simple osmotic effects are out of the question here. Overton came to essentially the same conclusion and attempted to help out the problem by his conceptions of lipoidal membranes about living cells and their entire impermeability to salts. He showed conclusively in his work that Loeb's explanation of the action of acids and alkalies cannot be correct, for were all the proteins, carbohydrates, and fats contained in muscle, split into their simplest digestion products they would still not yield a sufficient number of molecules to account, through conceptions of osmotic pressure, for the amount of water absorbed

[1] University of Chicago Decennial Publications, 1902, x; cited from a reprint.
[2] Pflüger's Archiv f. d. ges. Physiologie, 1902, xcii, 115.

by muscle in the solution of an acid or an alkali. To the details of Overton's ideas we shall have occasion to return later.

In detailed experimental results and in the conclusions drawn from them there exist many contradictions between the findings of these various authors. It is needless to touch upon them in detail. For a majority of these differences an explanation can readily be found. None of the authors mentioned ever studied the *curves* of absorption of water by muscle under various conditions. They weighed their muscles at arbitrary intervals of time, and drew their conclusions from these weighings — at times only one weighing. A moment's study of a few of the curves which accompany this article will show how wrong this is. (See Figures 31 to 33.) To cite but one example, a muscle kept in any salt solution need not, and, in fact, usually does not, show a progressive increase or decrease in weight. It may at first show a very decided decrease and later an equally decided increase; or the reverse may be the case. If this fact is borne in mind, many of the statements made by these authors and not in harmony with each other or with my own experimental results will find a ready explanation.

We will turn now to the conclusions to which I have been led from my own experiments, and see if in them we may not find an acceptable explanation of the apparently unattached and not easily accounted for facts observed by the previous workers in this field. My experiments were made with the hind legs of tree toads (Hyla) from which the skin had been removed, and with the gastrocnemius muscles of the frog (Rana). The muscle preparations were carefully dried, weighed, and placed in various solutions contained in lightly covered finger bowls. At various intervals they were removed from the solutions, carefully dried with filter paper, and weighed, and the amount of water they had lost or gained was calculated in per cent. of the original weight of the muscle. From many such experiments the following conclusions of importance to the subject in hand were drawn. The conclusions are again lettered so as to permit ready comparison with similarly lettered and corresponding conclusions

reached in the study of the absorption of water by fibrin and by gelatine.

a) A muscle swells more in the solution of any acid than it does in pure water, but the amount of this swelling is greater in some acids than in others. Muscle swells most in a hydrochloric acid solution, almost as much in a nitric acid solution of the same concentration, and less in acetic and sulphuric acids

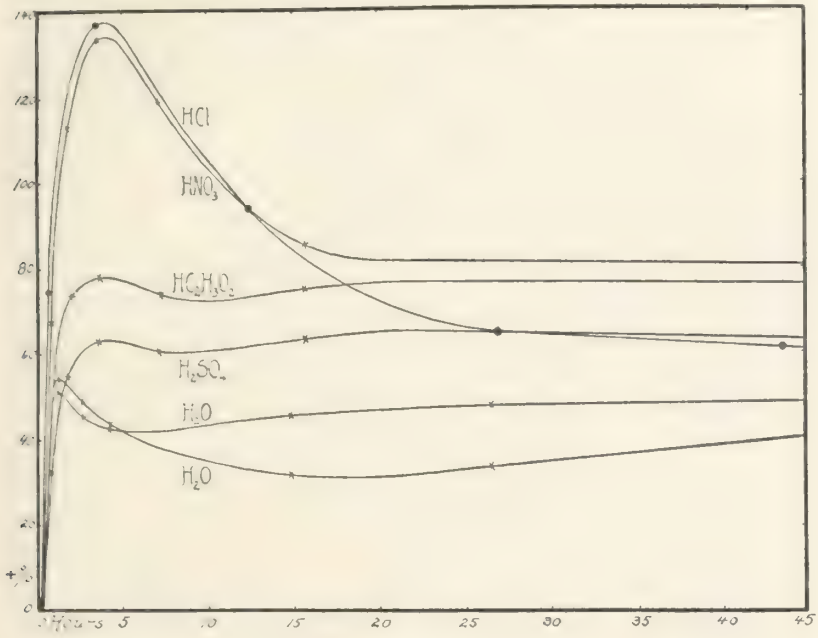


FIGURE 27

in the order named. Figure 27 may serve as an illustration of this fact. The experiments upon which these curves are based were made with the hind legs of tree toads (Hyla) from which the skin had been removed.[1]

An important relationship exists between the concentration of the acid employed and the amount that the muscle will swell.

[1] Martin H. Fischer, Pflüger s Archiv f. d. ges. Physiologie, 1908, cxxiv, 69.

This is readily apparent from Figure 28 and Table O, which contains the experimental findings from which the curves were

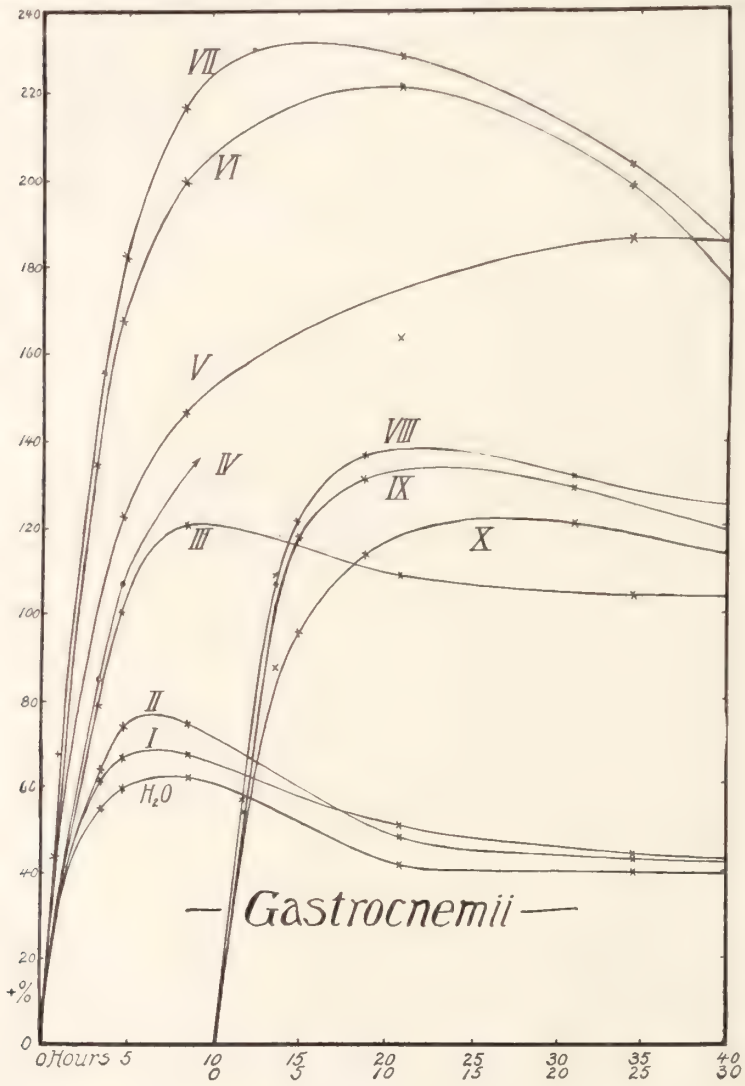


FIGURE 28

constructed. The table is given in detail to show by what means all the data upon which the conclusions of this section are based

were obtained. In the series of experiments shown in Figure 28, the gastrocnemius muscles of frogs (Rana) were used. At first we note an increase in the amount of the swelling with every increase in the concentration of the acid. But after a time a point is reached beyond which a further increase in concentration is followed by a diminished absorption of water. This fact has its analogue in the absorption of water by fibrin or gelatine in acid solutions of various concentrations.

In the following Table O the first figure in each of the columns indicates the original weight of the muscle. After each of the weighings there is given, in parentheses, the gain in weight, expressed in per cent. of the original weight of the muscle.

(*b*) It is somewhat difficult to say what is the effect of alkalies on the absorption of water by muscle. The statement is unquestionably true that muscle swells more in the solution of any alkali than in water. There seems to be a great difference, however, in the swelling of tree toad legs from which the skin has been removed, or of the gastrocnemii muscles of frogs, not only as regards the individual muscle preparations, but with the season. In my original experiments with tree toads I got a decidedly greater swelling in dilute alkaline solutions than in water. In some recent experiments (December 11, 1908) with the gastrocnemius muscles of winter frogs (Rana) this difference was not so marked. I append Tables P and Q to illustrate this point. In explanation of these results we must consider that the amount of swelling in pure water seems unusually high in these particular experiments. As this swelling is to my mind brought about solely through the production of acid within the muscles after removal from the body, the high water absorption values would indicate an unusually large production of acid. When such muscles are placed in alkaline solutions, the alkali combines with the acid, and the salt formed by this union inhibits the swelling. (See paragraph *d* below.)

TABLE O. *Gastrocnemius Muscles of the Frog.*

Hours in the solution.	110 c.c. H_2O.	1.4 c.c. 1/10 n. HCl + 109-3.4 c.c. H_2O.	1.2 c.c. 1/10 n. HCl + 109-1.2 c.c. H_2O.	1 c.c. 1/10 n. HCl + 109 c.c. H_2O.	2 c.c. 1/10 n. HCl + 108 c.c. H_2O.	3 c.c. 1/10 n. HCl + 107 c.c. H_2O.
	%	%	%	%	%	%
0	0.582 (0)	0.599 (0)	0.596 (0)	0.568 (0)	0.430 (0)	0.448 (0)
1.05	0.790 (+35.7)	0.829 (+38.4)	0.815 (+35.06)	0.781 (+ 34.0)	0.650 (+ 27.8)	0.699 (+ 56.0)
3.25	0.905 (+55.5)	0.965 (+61.1)	0.967 (+62.2)	1.015 (+ 78.6)	0.793 (+ 84.4)	0.915 (+104.2)
4.45	0.930 (+59.8)	0.990 (+65.2)	1.035 (+73.0)	1.137 (+100.1)	0.889 (+106.7)	0.999 (+123.1)
8.45	0.940 (+61.5)	0.998 (+66.6)	1.031 (+72.9)	1.259 (+121.6)	0.961 (+123.4)	1.102 (+146.0)
20.50	0.854 (+41.6)	0.908 (+51.6)	0.889 (+49.1)	1.200 (+111.2)	1.110 (+158.1)	1.178 (+162.9)
34.10	0.820 (+40.9)	0.860 (+43.5)	0.850 (+42.6)	1.165 (+105.1)	1.345 (+212.7)	1.280 (+185.6)
45.50	0.810 (+39.2)	0.850 (+41.9)	0.845 (+41.7)	1.155 (+103.3)	1.410 (+227.9)	1.260 (+181.2)
70.20	0.818 (+40.0)	0.835 (+39.4)	0.830 (+39.2)	1.170 (+106.0)	1.425 (+231.4)	1.075 (+139.9)
	(a)	(b)	(c)	(c)	(d)	(d)
	I		II	III	IV	V

Hours in the solution.	4 c.c. 1/10 n. HCl + 106 c.c. H_2O.	5 c.c. 1/10 n. HCl + 105 c.c. H_2O.	8 c.c. 1/10 n. HCl + 102 c.c. H_2O.	9 c.c. 1/10 n. HCl + 101 c.c. H_2O.	10 c.c. 1/10 n. HCl + 100 c.c. H_2O.
	%	%	%	%	%
0	0.491 (0)	0.541 (0)	0.723 (0)	0.686 (0)	1.021 (0)
1.05	0.815 (+ 65.9)	0.960 (+ 43.6)	1.138 (+ 57.4)	1.072 (+ 56.2)	1.520 (+ 48.8)
3.25	1.150 (+134.2)	1.387 (+156.3)	1.500 (+107.4)	1.435 (+109.1)	1.915 (+ 87.5)
4.45	1.313 (+167.4)	1.532 (+183.1)	1.595 (+120.6)	1.505 (+119.4)	2.008 (+ 96.6)
8.45	1.473 (+200.0)	1.720 (+217.9)	1.710 (+136.5)	1.586 (+131.1)	2.172 (+112.7)
20.50	1.578 (+221.3)	1.780 (+229.0)	1.675 (+131.6)	1.582 (+129.9)	2.248 (+120.1)
34.10	1.420 (+189.6)	1.650 (+204.9)	1.632 (+125.7)	1.458 (+112.5)	2.160 (+111.8)
45.50	1.220 (+148.4)	1.480 (+173.8)	1.585 (+119.2)	1.455 (+112.1)	2.130 (+109.5)
70.20	1.095 (+123.0)	1.285 (+137.5)	1.540 (+113.0)	1.370 (+ 99.7)	2.070 (+102.6)
	(e)	(e)	(f)	(f)	(g)
	VI	VII	VIII	IX	X

c, c. d, d. etc., indicate opposite muscles of same frog.

c Loeb states that the gastrocnemius muscles of frogs swell more in the solution of an alkali than in acid solutions of the same normality. While I believed this myself originally, the experiments just outlined leave the question still an open one. The few weighings that Loeb gives are not conclusive, for only serial weighings can tell us whether the maximal swelling in a muscle has been attained, is being approximated, or has been passed.

TABLE P.—*Gastrocnemius Muscles of the Frog.*

Hours in the solution.	110 c.c. H_2O.	5 c.c. 1/10 n. NaOH + 105 c.c. H_2O.	10 c.c. 1/10 n. NaOH + 100 c.c. H_2O.
	%	%	%
0	0.984 (0)	0.571 (0)	0.571 (0)
1.05	1.397 (+41.9)	0.858 (+50.2)	0.920 (+ 61.1)
3.25	1.610 (+63.6)	0.995 (+56.7)	1.104 (+ 93.3)
4.45	1.659 (+68.5)	0.881 (+54.3)	1.144 (+100.3)
8.45	1.680 (+70.7)	0.854 (+49.5)	1.141 (+ 99.8)
20.50	1.626 (+65.2)	0.842 (+47.4)	1.108 (+ 94.04)
34.10	1.540 (+56.5)	0.838 (+45.9)	1.125 (+ 97.0)
45.50	1.530 (+55.4)	0.850 (+48.1)	1.142 (+100.0)
70.20	1.510 (+53.4)	0.885 (+54.9)	1.135 (+ 98.7)

d The addition of any salt to the solution of an acid decreases the amount that a muscle will swell in that solution; and the higher the concentration of the salt, the greater is the amount of this inhibition. Figure 29 illustrates this fact. The curve marked HCl was obtained by immersing a gastrocnemius muscle in a solution of hydrochloric acid, made by adding 10 c.c. $\frac{1}{10}$ normal hydrochloric acid to 100 c.c. of water. The three remaining curves show the changes in weight suffered by muscles immersed in solutions made by adding the same amount of acid to 100 c.c., respectively, of a $\frac{1}{8}$, $\frac{1}{4}$, or $\frac{1}{2}$ molecular solution of sodium chloride. As is plainly evident, the action of the hydrochloric acid is entirely inhibited, so far as the absorption of water is concerned when the last-named concentration of sodium chloride is employed.

TABLE Q.—*Gastrocnemius Muscles of the Frog.*

Hours in the solution.	110 c.c. H_2O.	1/4 c.c. 1/10 n. NaOH + 109·3 4 c.c. H_2O.	1·2 c.c. 1·10 n. NaOH + 109·1·2 c.c. H_2O.	1 c.c. 1·10 n. NaOH + 109 c.c. H_2O.	2 c.c. 1·10 n. NaOH + 108 c.c. H_2O.	3 c.c. 1·10 n. NaOH + 107 c.c. H_2O.	4 c.c. 1·10 n. NaOH + 106 c.c. H_2O
	%	%	%	%	%	%	%
0	0·808 (0)	0·732 (0)	0·706 (0)	0·704 (0)	0·609 (0)	0·608 (0)	0·595 (0)
1·00	1·104 (+36·6)	1·022 (+39·6)	0·970 (+37·4)	0·972 (+38·0)	0·882 (+44·8)	0·905 (+48·8)	0·852 (+43·2)
3·50	1·265 (+56·5)	1·150 (+57·1)	1·090 (+54·4)	1·106 (+57·1)	0·900 (+47·8)	0·893 (+46·87)	0·875 (+48·7)
6·35	1·300 (+73·2)	1·170 (+59·8)	1·100 (+55·8)	1·120 (+59·1)	0·860 (+41·2)	0·870 (+43·1)	0·840 (+48·7)
8·50	1·290 (+59·6)	1·155 (+57·8)	1·072 (+51·8)	1·102 (+56·5)	0·849 (+38·0)	0·855 (+40·6)	0·818 (+37·5)
11·30	1·260 (+55·9)	1·130 (+54·3)	1·048 (+48·4)	1·070 (+51·9)	0·858 (+40·8)	0·865 (+42·1)	0·820 (+37·8)
24·30	1·135 (+40·4)	1·030 (+40·7)	0·950 (+34·5)	0·975 (+38·5)	0·884 (+45·1)	0·908 (+49·3)	? ?
34·50	1·140 (+41·0)	1·032 (+40·98)	0·970 (+37·4)	0·995 (+41·2)	0·920 (+51·0)	0·935 (+53·78)	0·872 (+46·5)
58·45	1·130 (+39·8)	1·028 (+40·4)	0·965 (+36·7)	1·000 (+42·04)	0·920 (+51·0)	0·935 (+53·78)	0·875 (+47·05)
82·40	1·130 (+39·8)	1·015 (+38·6)	0·965 (+36·7)	1·040 (+47·7)	0·925 (+52·0)	0·940 (+54·6)	0·885 (+48·7)

Hours in the solution.	5 c.c. 1/10 n. NaOH + 105 c.c. H_2O.	6 c.c. 1/10 n. NaOH + 104 c.c. H_2O.	7 c.c. 1·10 n. NaOH + 103 c.c. H_2O.	8 c.c. 1·10 n. NaOH + 102 c.c. H_2O.	9 c.c. 1·10 n. NaOH + 101 c.c. H_2O.	10 c.c. 1·10 n. NaOH + 100 c.c. H_2O.	110 c.c. H_2O.
	%	%	%	%	%	%	%
0	0·580 (0)	0·558 (0)	0·547 (0)	0·545 (0)	0·537 (0)	0·461 (0)	0·447 (0)
1·00	0·885 (+52·6)	0·818 (+46·5)	0·795 (+45·3)	0·890 (+63·3)	0·778 (+44·8)	0·675 (+46·4)	0·655 (+46·5)
3·50	0·918 (+58·3)	0·822 (+47·3)	0·835 (+52·65)	0·935 (+71·5)	0·813 (+51·4)	0·710 (+52·0)	0·715 (+59·9)
6·35	0·900 (+55·2)	0·795 (+42·5)	0·820 (+49·9)	0·910 (+66·9)	0·795 (+48·0)	0·680 (+47·5)	0·705 (+57·7)
8·50	0·880 (+51·7)	0·789 (+41·0)	0·802 (+46·6)	0·912 (+67·3)	0·796 (+48·2)	0·670 (+45·3)	0·680 (+52·1)
11·30	0·855 (+47·4)	0·770 (+37·8)	0·800 (+46·25)	0·900 (+65·1)	0·778 (+44·9)	0·660 (+43·1)	0·642 (+43·6)
24·30	0·825 (+42·2)	0·845 (+51·4)	0·790 (+44·4)	0·920 (+68·8)	0·825 (+53·6)	0·670 (+45·3)	0·605 (+35·3)
34·50	0·880 (+51·7)	0·825 (+47·8)	0·840 (+53·5)	0·990 (+81·6)	0·870 (+58·0)	0·725 (+57·2)	0·620 (+38·7)
58·45	0·900 (+55·2)	0·830 (+48·7)	0·860 (+57·2)	1·020 (+87·1)	0·910 (+69·5)	0·755 (+63·7)	0·610 (+36·4)
82·40	0·900 (+55·2)	0·845 (+51·4)	0·863 (+57·5)	1·030 (+88·9)	0·925 (+72·2)	0·772 (+67·4)	0·605 (+35·3)

(c) While all salts diminish the amount of water absorbed by muscle in an acid solution, the different salts are very unequally effective in this regard, when equimolecular solutions are compared. The effect of three acetates on the swelling of tree toad musculature is compared in Figure 30. The upper curve represents the action of a pure $\frac{1}{110}$ normal hydrochloric acid solution,

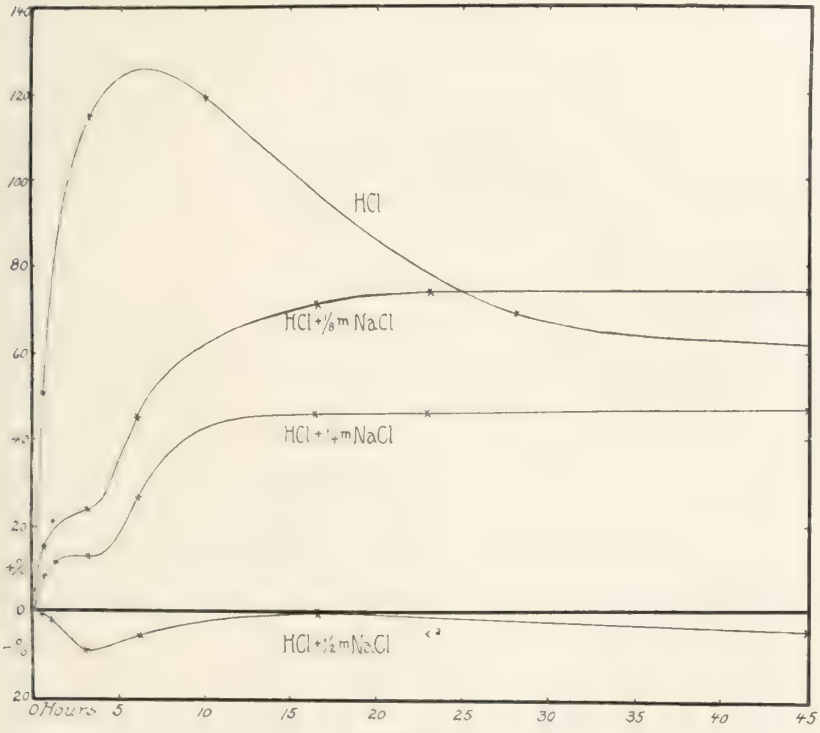


FIGURE 29

made by adding 10 c.c. $\frac{1}{110}$ normal hydrochloric acid to 100 c.c. water; the remaining curves, the effect when the same amount of acid is added, respectively, to 100 c.c. $\frac{1}{4}$ molecular solutions of potassium, sodium, and calcium acetate. We have no difficulty in recognizing that these salts are effective in reducing the amount of swelling in the order named, potassium being less powerful

than sodium, and this than calcium. It will be remembered that we found the same arrangement of ions when the action of different salts with a common anion on the swelling of fibrin in acid solutions was compared.

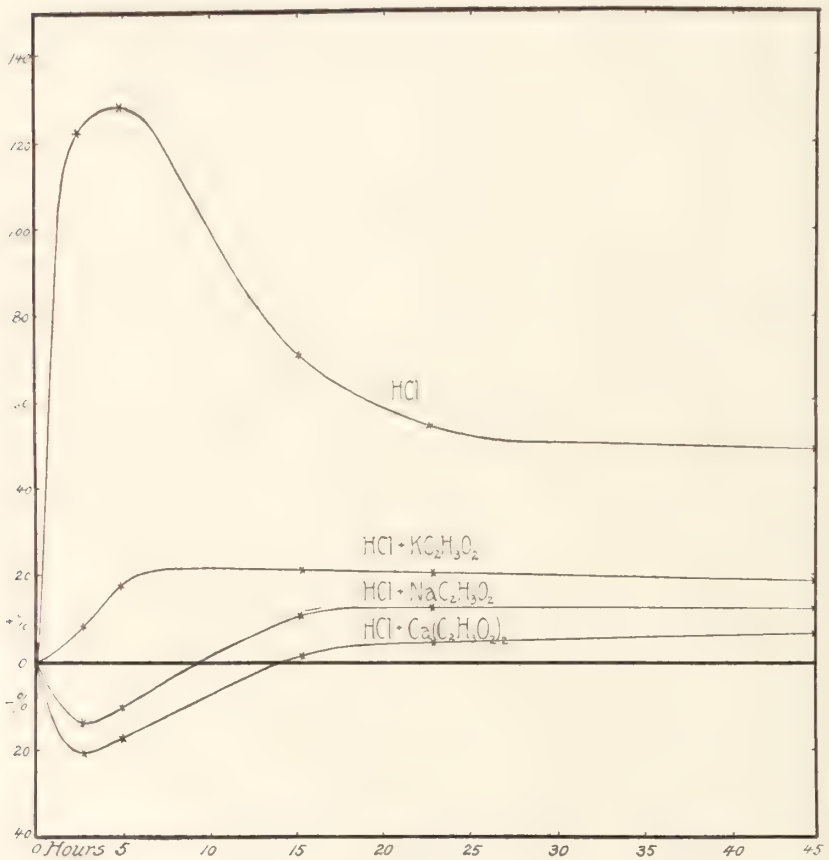


FIGURE 30

In Figure 31 are compared the effects of a series of chlorides on the swelling of muscle in acid solutions. The hydrochloric acid curve stands prominently above that for pure water. All the salts bring about a diminution in the amount of swelling of the muscle, but while present in the same molecular concentration

they are very differently effective in this regard. The solutions were all prepared by adding 10 c.c. $\frac{1}{10}$ normal hydrochloric acid to 100 c.c. $\frac{1}{4}$ molecular solutions of the various salts. We have

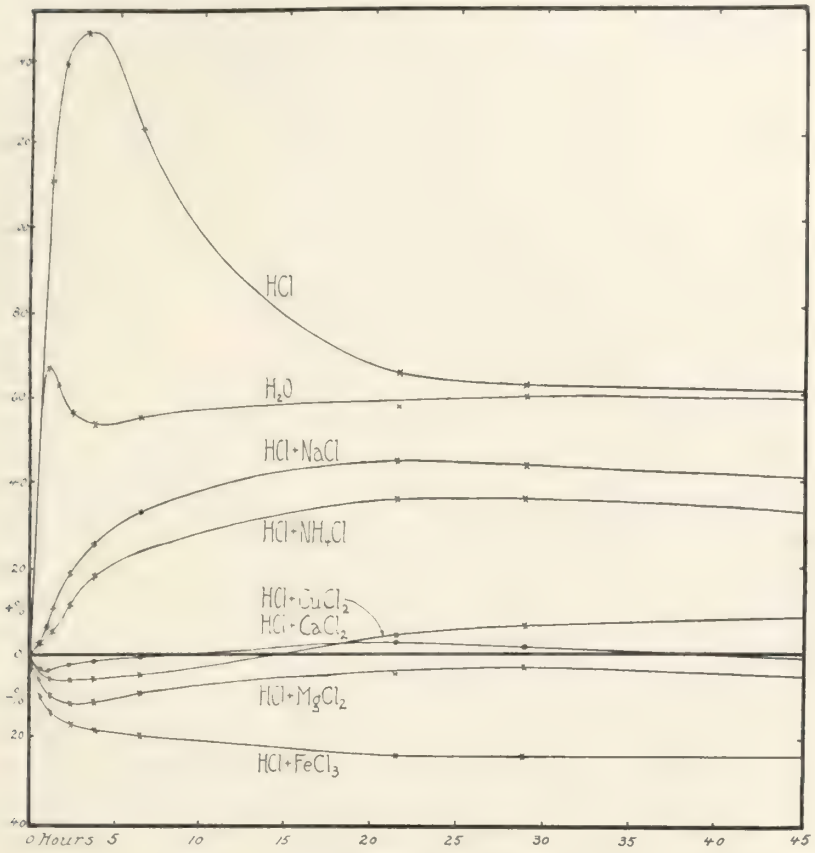


FIGURE 31

no difficulty in recognizing the following order in which the different ions are effective, that producing the least inhibition being given first:

Sodium, Ammonium, Calcium, Copper (ic), Magnesium, Iron (ic).

The general grouping of these ions is very similar to that given for the kations in our study of the effects of different salts on

the swelling of fibrin. That the arrangement of the individual ions is not identical in the two series is not surprising, for muscle represents not only a mixture of several colloids, but contains several salts. It is, therefore, from both a physical and a chemical standpoint a substance not nearly so well defined as washed fibrin obtained from blood.

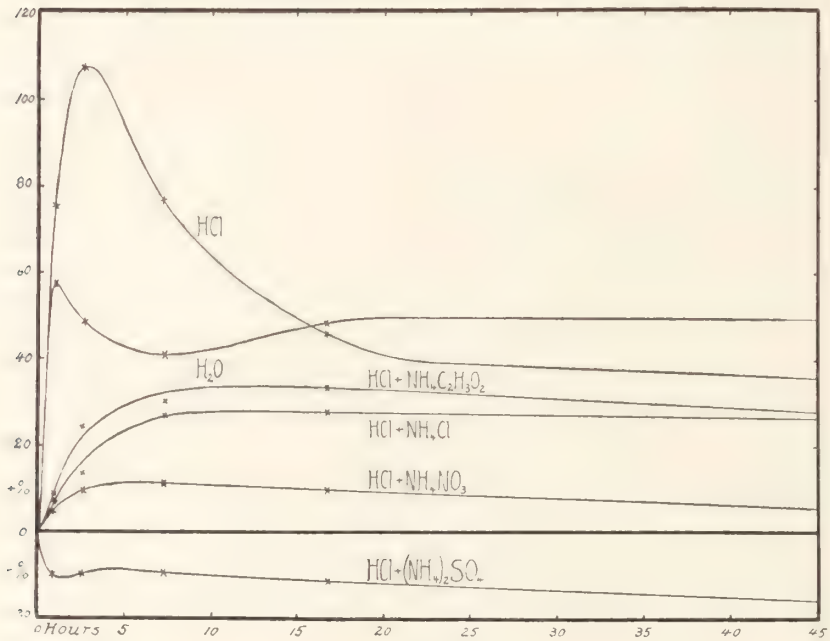


FIGURE 32

Figure 32 permits the comparison of a few anions. The curves for hydrochloric acid and for water need no special comment. The solutions containing salts were again prepared by adding 10 c.c. $\frac{1}{10}$ normal hydrochloric acid to 100 c.c. of the $\frac{1}{4}$ molecular solutions of the required ammonium salts. The order:

Acetate, Chloride, Nitrate, Sulphate,

in which the ion least effective in reducing the swelling of muscle in an acid solution is named first, is readily recognized. The general grouping of these is again the same as in the case of fibrin.

The relations in muscle are not, however, all as simple as might at first appear from the analogy between the swelling of fibrin and the swelling of muscle as described above. Figure 33 has been introduced in illustration of this fact. A number of anions may here be compared, but as is readily apparent, the order in which this series of sodium salts is effective is not an easy one to

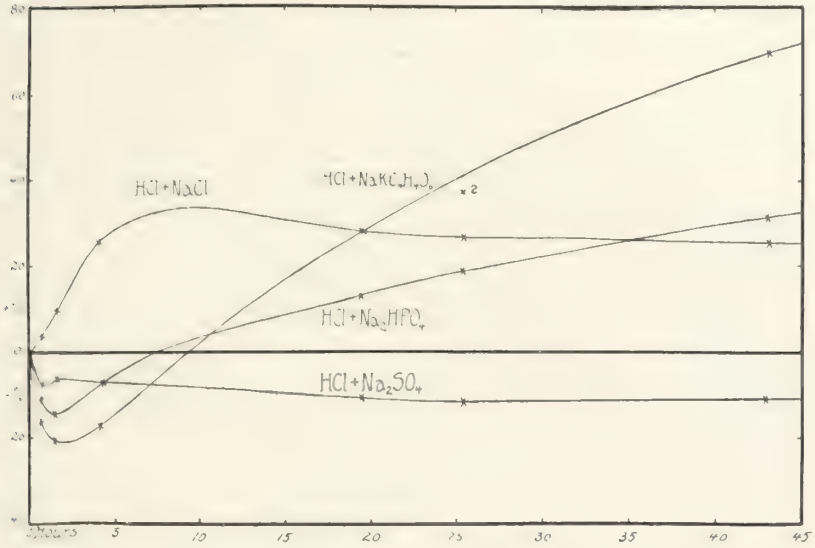


FIGURE 33

describe. We recognize in the first few hours of the experiment the order familiar to us from our study of fibrin,

Chloride, Sulphate, Phosphate, Tartrate,

but in the later hours this is changed to

Tartrate, Phosphate, Chloride, Sulphate.

The causes for this change are not as yet clear. They are undoubtedly several in number, dependent in part on differences in diffusion of acids, salts, etc., into and out of the muscles; in part, on the fact that muscle after removal from the body under-

goes spontaneously a series of chemical changes through which its physical state is progressively altered. This series of curves shows very well the dangers inherent in conclusions based upon single or too few weighings of muscle at arbitrarily chosen intervals.

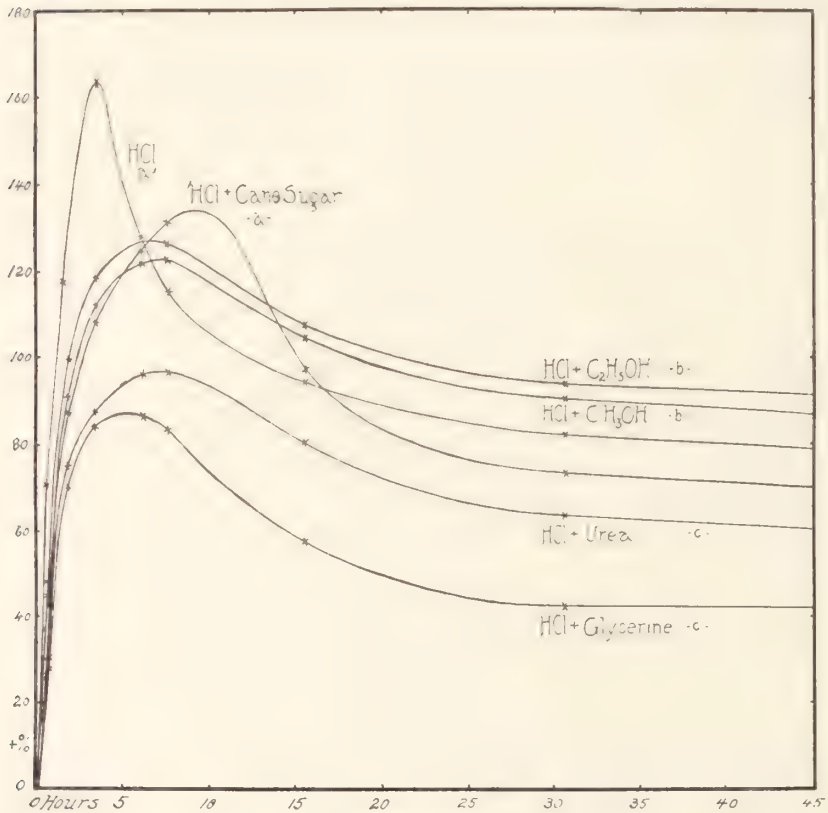


FIGURE 34

(*f*) The marked effect of all electrolytes in reducing the amount that a muscle will swell in an acid solution is not shared by non-electrolytes. Figure 34 shows this better than many words. None of the curves show any characteristic change in shape from the pure hydrochloric acid curve in spite of the fact that the various non-electrolytes are present in amounts *osmotically* more

than equal to those of the electrolytes used in the already described experiments. In each case 10 c.c. of a $\frac{1}{10}$ normal hydrochloric acid solution were added to 100 c.c. of a $\frac{1}{2}$ molecular solution of cane sugar, ethyl or methyl alcohol, urea or glycerine. While I do not wish to contend that the non-electrolytes are entirely without effect — it will be remembered that they influenced somewhat the swelling of pure gelatine in acid solutions — I question whether the effect apparent in Figure 34 is really as great as it seems. The curves marked with the same letter indicate opposite members of the same pair of tree toad legs, and from their close association the impression is received that the individual variations in the muscles may have contributed not inconsiderably toward their general arrangement in the drawing.

g) The taking up and giving off of water by muscle represents in large part a reversible process. This process, however, is not completely reversible (within the time limits of these experiments) in that a muscle seems to suffer a somewhat permanent change from every condition through which it is required to pass. This statement, which is entirely analogous to that made regarding the behavior of fibrin, is illustrated in Figure 35. The first part of the curve *a*, *a*, *a*, represents the stage of progressive loss of water by a gastrocnemius muscle which has passed the point of maximal swelling in a solution of $\frac{1}{110}$ normal hydrochloric acid. At the point indicated by the small arrow it is transferred to pure water, in which the muscle is observed to gain promptly in weight and so continue for some hours. An explanation of this fact is readily found when we look at Figure 28 and Table O. A $\frac{1}{110}$ normal hydrochloric acid solution does not represent the optimal concentration for the swelling of a frog's muscle, and to remove it from such a solution and place it in pure water is to place the muscle, at least for a time, under conditions which approximate those optimal for the swelling of muscle more nearly (an acid solution below the concentration of a $\frac{1}{110}$ normal).

Curve *b*, *b*, *b*, *b*, represents the effect of transference from a mixture of acid and potassium chloride, to one of acid and calcium chloride, and finally into a pure hydrochloric acid solution.

While the muscle was steadily increasing in weight in the HCl-KCl mixture, it began to lose immediately after transfer to the HCl-$CaCl_2$ mixture. When taken out of this solution and placed in pure HCl, a gain is noted, but this is not sufficiently great to make the muscle even approximate in weight that originally

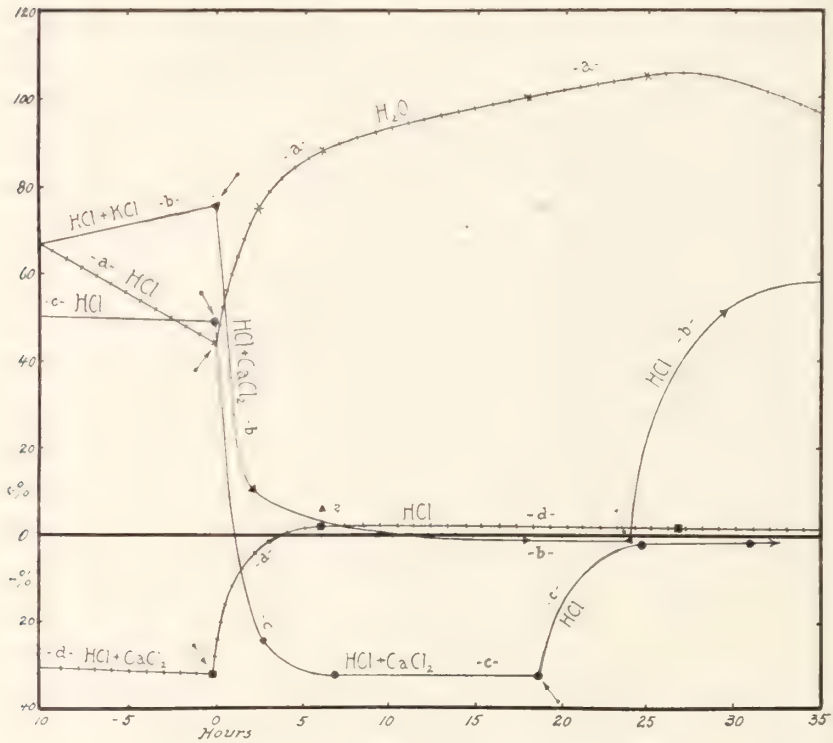


FIGURE 35

attained in the HCl–KCl mixture—the muscle does not recover entirely from the effect of residence in the hydrochloric acid solution which contains calcium chloride.

Curve *c*, *c*, *c*, *c*, indicates also the somewhat lasting effect upon the muscle of every condition through which it has passed. The sharp fall in weight upon transference of the muscle from the pure $\frac{1}{110}$ normal hydrochloric acid solution to an equally con-

centrated one containing calcium chloride (10 c.c. $\frac{1}{10}$ normal HCl + 100 c.c. $\frac{1}{2}$ molecular $CaCl_2$) and the only incomplete restitution when returned to the pure acid solution is clearly evident in the drawing.

In curve *d*, *d*, *d*, is found additional evidence for the incomplete reversibility of the absorption and secretion of water by muscle. The muscle had steadily lost in weight since being placed in a mixture of 10 c.c. $\frac{1}{10}$ normal HCl + 100 c.c. $\frac{1}{2}$ molecular $CaCl_2$ when at the point indicated by the small arrow it was transferred to a pure $\frac{1}{10}$ normal hydrochloric acid solution. The muscle began to gain immediately, but owing to previous residence in the solution containing calcium chloride this gain amounted to little more than a restoration of the original weight of the muscle.

(*h*) A final word is necessary regarding the *quantitative* relationship between the amount of water absorbed by a colloid and the amount absorbed by muscle. In other words, we have to discover whether the absorption of water by such a colloid as fibrin is of sufficient magnitude to account, without strain, for the maximal amounts ever absorbed by muscle. The largest amount of water that I ever found to be absorbed by any muscle in my experiments was less than two and one-half times the original weight of the muscle (246.6 per cent.). As fresh muscle contains about 75 per cent. of water and only 1 per cent. ash, we may say, roughly, that about one-fourth of the weight of muscle consists of various organic substances. These belong, nearly all of them, to the group of the colloids, and into that special half of the colloids which we have called hydrophilic or emulsion colloids. On the basis of these figures one gram of *dried* muscle substance is equivalent to four grams of moist (normal) muscle, which has the power of absorbing enough water (250 per cent.) to weigh fourteen grams. According to these figures, one part of *dry* muscle substance may absorb thirteen times its weight of water. How easily this, which represents the extreme of water absorption in muscle, may be accounted for through the power of simple colloids to absorb water, is apparent when it is stated that fibrin readily absorbs ten to twenty times its weight of water

in dilute acids and as much as thirty (under the best circumstances almost forty) times its weight in dilute alkalies. The maximal values obtained with gelatine are not as high as in the case of fibrin, but even this absorbs without difficulty fifteen to twenty-five times its weight of water.

This extensive analogy between the absorption of water by fibrin or gelatine and the absorption of water by muscle, both from a quantitative and a qualitative standpoint, seems to me to justify the conclusion that *the absorption of water by muscle is determined in the main by the state of the colloids contained in the muscle.* But since fibrin and gelatine are merely examples of a special group of colloids, and muscle only a tissue chosen at random for study, the question naturally arises: Is the absorption of water by all tissues simply a function of the state of the colloids they contain? We will next attempt to answer this larger question, and in doing so we will become acquainted with experimental facts which we will discover to be of material help to us in our further consideration of the problem of œdema.

2. The Analogy between the Absorption of Water by Certain Colloids and the Absorption of Water by the Eye.

The eye consists, as is well known, of a series of different tissues, the individual physical characteristics of which differ markedly from each other. There is no difficulty in distinguishing between the opaque sclera, the clear and transparent cornea, the well-named "glass-like" vitreous, and the lens. The eye, in consequence, represents a collection of tissues which may be utilized as experimental material in our attempt to see if the analogy between the absorption of water by certain colloids and the absorption of water by muscle, cannot be broadened to embrace an analogy between the absorption of water by these colloids and the absorption of water by protoplasm in general.

The following experiments show very clearly that *the absorption of water by the eye is governed by the same laws as the absorp-*

tion of water by fibrin or gelatine. In these experiments the eyes of sheep, pigs, and cattle were employed shortly after their removal from the animals at the slaughter house. For the most part sheep eyes were used, but identical results can be obtained with the eyes of pigs or cattle. To avoid useless details only the conclusions from many series of experiments are given below, and these have been arranged in lettered paragraphs which correspond with similarly lettered ones in the section on the swelling of fibrin and the swelling of gelatine. In this way what has been said of fibrin and gelatine may easily be compared with what is said regarding the absorption of water by the eye.[1]

Let it be added that the eyes had all been carefully trimmed of adhering tags of muscle and fat, and that the amount of the absorption of water was determined by weighing the eyes at various intervals, and calculating the increase or decrease in weight in percentage of the original weight of the fresh (moist) eyes. The eyes were kept in lightly covered finger bowls containing enough of the various solutions to cover the eyes. 200 c.c. are about sufficient for sheep eyes, while the large cattle eyes demand 300 c.c. To carry out the weighings the eyes were taken out of their solutions, carefully dried with soft filter paper, and weighed as quickly as possible on balanced powder papers, such as are employed by pharmacists.

The following conclusions are of importance in our discussion:

(*a*) An enucleated eye absorbs more water in the solution of any acid than in distilled water, but when equinormal acids are compared these are found to be unequally effective in this regard. Figure 36 shows graphically the results of a few such experiments with $\frac{1}{10}$ normal acids. As is easily apparent, the swelling in hydrochloric and nitric acids is sufficiently great to lead to a rupture of the eyeball—the sclera splits and allows the escape of the more fluid contents of the eye. Rupture of the eyeball is indicated in this figure and in all that follow by the five-cornered star at the end of the curves. Sulphuric, oxalic, and acetic acids are

[1] For detailed weighings and figures, see Martin H. Fischer, Pflüger's Archiv f. d. ges. Physiologie, 1908, cxxv, 396, and ibid., 1909, cxxvii, 1.

all less potent in making eyes swell, for the absorption curves with these acids are decidedly lower, in the order named, than those for nitric and hydrochloric acids. In none of these does

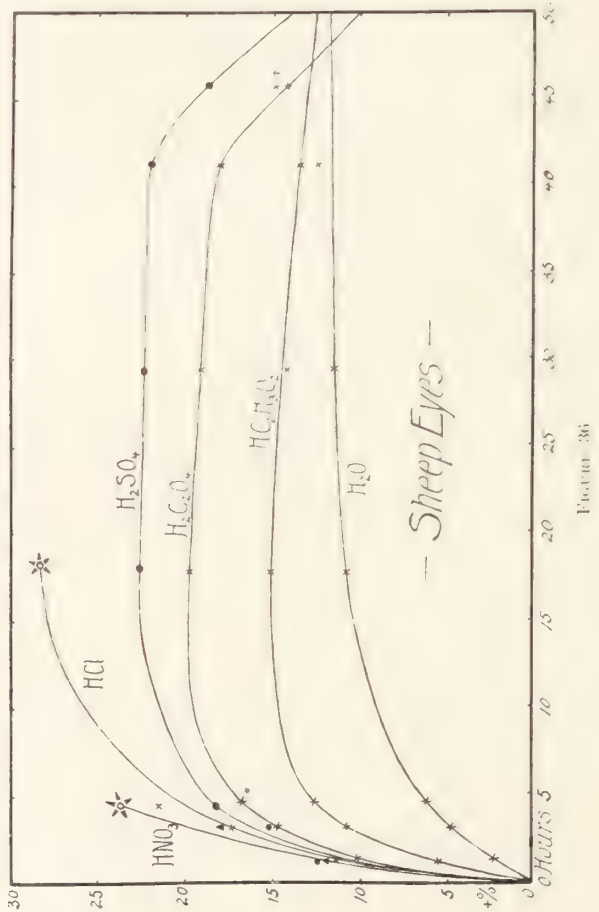


FIGURE 36

a rupture of the eyes occur at the concentrations employed. The curve obtained by immersion of an eye in pure water is introduced for comparison.

The amount that an eye swells in any acid solution is dependent on the concentration of the acid. This is illustrated in Figure 37.

The curve for pure water is the lowermost one. The Roman numerals indicate progressively higher concentrations of hydrochloric acid. The solutions were made by adding 2, 4, 6, 8, 12, 14, and 16 c.c. of a $\frac{1}{10}$ normal hydrochloric acid to enough water to make 220 c.c. of solution. The acid solutions vary in consequence from (approximately) a $\frac{1}{1100}$ normal to a $\frac{1}{110}$ normal.

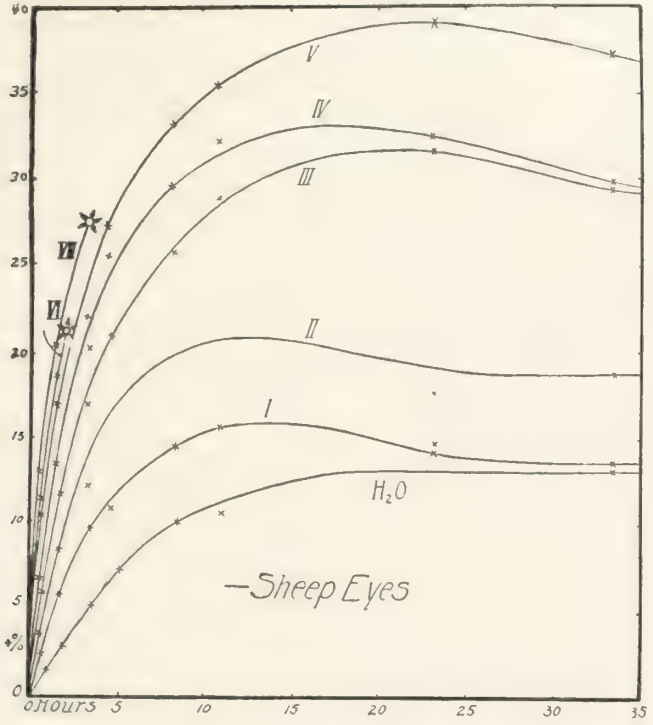


FIGURE 37

A definite increase in the amount of swelling with every increase in concentration is readily discernible. In the highest concentrations the absorption of water is sufficiently great (and sufficiently rapid) to lead to rupture of the eye.

It is of extreme interest to note how low a concentration of acid brings about a decided absorption of water by the eye. The

lowest concentration of hydrochloric acid in this series does not betray its acid character to the sense of taste; the second has a taste but it cannot be recognized as sour. It requires imagination to recognize the acid taste even in the third concentration in which an eye becomes stony hard.

(*b*) Eyes swell more in the solution of an alkali than in pure water. While there is no question about this fact (see Figure 38), the amount of difference in swelling between an eye in pure water and one in the solution of an alkali is not as great as that between an eye in water and one in an acid solution. The same explanation probably holds for this observation as was given for the difference in the amount of swelling of muscle in solutions of acids and alkalies. The eye after removal from the body undergoes a spontaneous acid change. This acid is neutralized by the alkali of the solution into which the eye is dropped, whereby a salt is formed, the presence of which inhibits the swelling of the eye in the alkaline solution. (See paragraph *d* below.)

The different alkalies affect the swelling of the eyes to unequal degrees when equinormal solutions are compared, but the exact order in which these different alkalies are effective is not yet definitely settled.

(*c*) If the amounts are compared that an eye will swell in acid and in alkaline solutions having, respectively, the same H or OH concentration, it is found that an eye swells *less* in the solution of an alkali than in an equally concentrated solution of an acid. The probable cause for this divergence from the behavior of fibrin has already been touched upon in the preceding paragraph.

(*d*) The presence of any salt in the solution of an acid or an alkali reduces the amount that an eye will swell in that solution. Figure 38 illustrates this fact as well as Figures 39, 40, and 41. In Figure 38 is easily noted the great difference in the amount of swelling induced in eyes through the action of equinormal solutions of acids and alkalies. The solutions of HCl and KOH are both $\frac{1}{110}$ normal made by adding 20 c.c. of a $\frac{1}{10}$ normal hydrochloric acid or potassium hydroxide solution to 200 c.c. of water. When an eye is placed in solutions made by adding the same

amounts of acid or alkali, respectively, to 200 c.c. $\frac{1}{4}$ molecular solutions of calcium chloride or sodium chloride, the curves marked HCl + $CaCl_2$ and KOH + NaCl are obtained. The curve of absorption in pure water is introduced as a control.

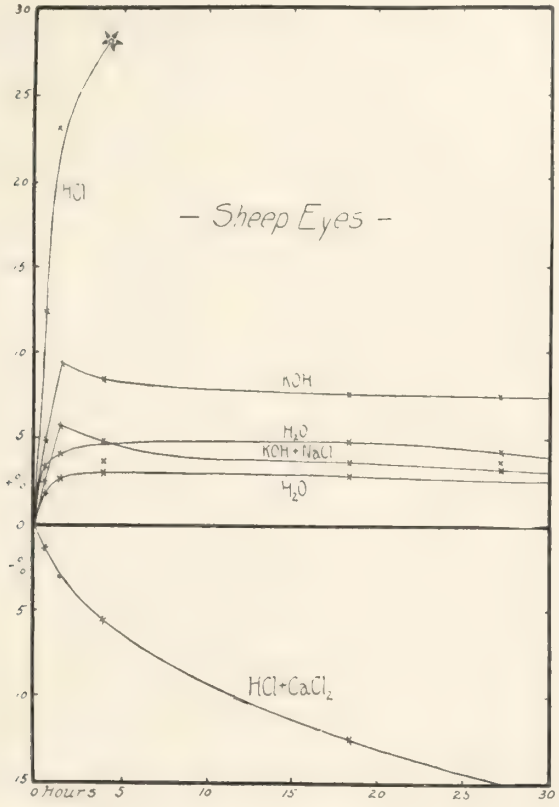


FIGURE 38

Figure 39 shows that the higher the concentration of the added salt the less does an eye swell in an acid solution. The eye bursts in the pure hydrochloric acid solution made by adding 20 c.c. $\frac{1}{10}$ normal hydrochloric acid to 200 c.c. of water. The remaining curves are self explanatory if it is stated that 20 c.c.

$\frac{1}{10}$ normal hydrochloric acid are added in each of these cases to 200 c.c. of the appropriate solution of calcium nitrate.

(c) When the effect of equimolecular solutions of different salts on the absorption of water by eyes in acid solutions is compared, it is found that the different salts are very unequally effective in this regard. As in the case of fibrin, the effect of any salt seems to be made up of the sum of the effects of its constituent ions.

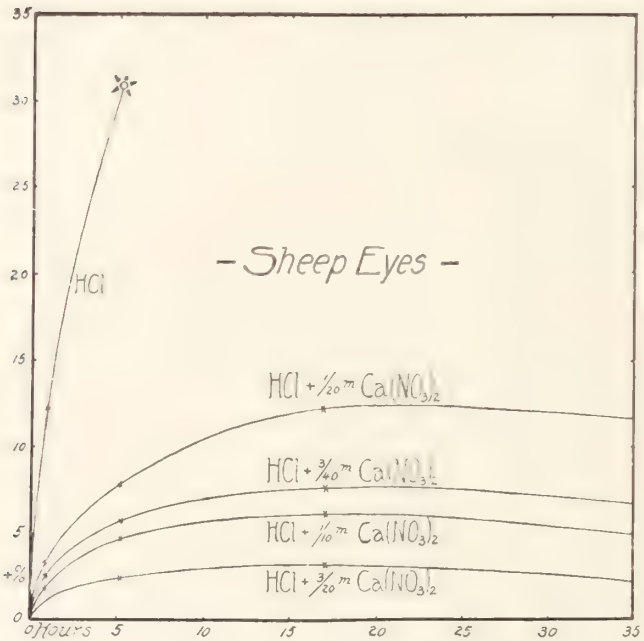


FIGURE 39

Figure 40 permits the comparison of the action of different *kations*. The eyes burst in both of the pure hydrochloric acid solutions. This occurred in none of those to which a salt had been added. These solutions containing salt were all made by adding 20 c.c. $\frac{1}{10}$ normal hydrochloric acid to 200 c.c. $\frac{1}{6}$ molecular solutions of the different chlorides. The ions arrange themselves in about the following order, in which that least effective in reducing the

amount of swelling in an acid solution is placed highest in the series, and first in each group:

1. Lithium, Ammonium, Potassium, Sodium.
2. Barium, Strontium, Magnesium, Calcium, Copper (ic).
3. Iron (ic).

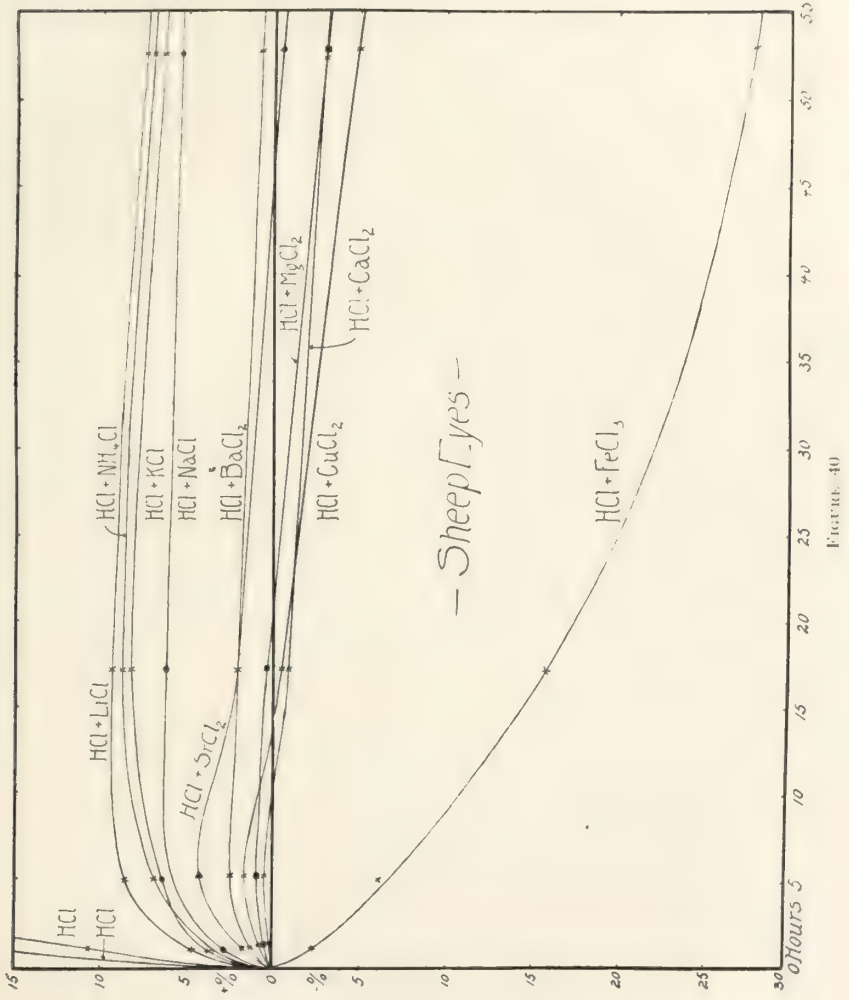


FIGURE 40

We have small difficulty in discovering in this table the same grouping of ions familiar to us from our discussion of the swelling of fibrin.

In Figure 41 are shown the effects of different *anions*. In each case 20 c.c. $\frac{1}{10}$ normal hydrochloric acid are again added to 200 c.c. of a $\frac{1}{6}$ molecular solution of the appropriate sodium

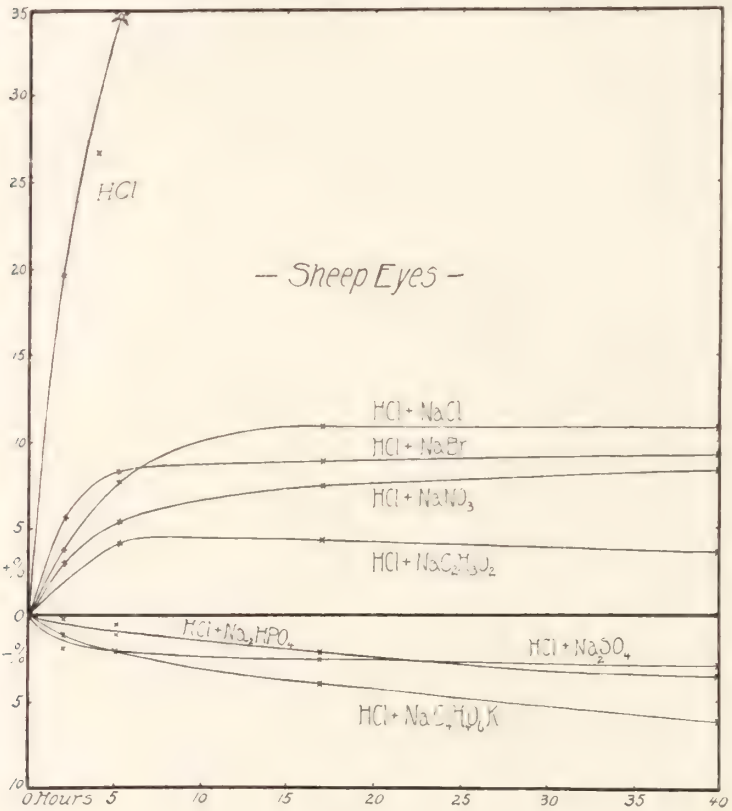


FIGURE 41

salt. The order of the ions is as follows in which that least effective in reducing the amount of swelling in an acid solution is placed first.

1. Chloride, Bromide, Nitrate, Acetate.
2. Phosphate, Sulphate, Tartrate.

This table is to all intents and purposes identical with that given in the discussion of the absorption of water by fibrin.

(*f*) Non-electrolytes do not share with electrolytes their marked power of influencing through their presence the absorption of water by the eye. Figure 42 shows this better than many words. The curves lie very closely together, and in spite of the fact that the various non-electrolytes are present in amounts which are *osmotically* more than equivalent to the powerfully acting electro-

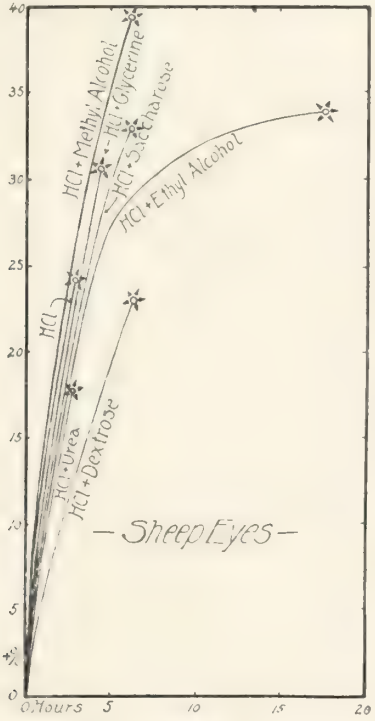


FIGURE 42

lytes (20 c.c. $\frac{1}{10}$ normal HCl + 200 c.c. $\frac{1}{3}$ molecular solution of the non-electrolyte), not one of the eyes has been kept from bursting.

(*g*) The absorption and secretion of water by the eye is to a large extent a reversible process. This is indicated in Figure 43. Curve A shows how an eye which has reached the bursting point in a pure hydrochloric acid solution suffers a prompt loss of water if taken out of this solution and transferred to an equally con-

centrated one containing calcium chloride in addition to the hydrochloric acid. Curve B shows the reverse of this process. An eye which has gained but little weight in pure water is transferred to a dilute hydrochloric acid solution. Immediately the absorption of water is hastened, and becomes so great that the

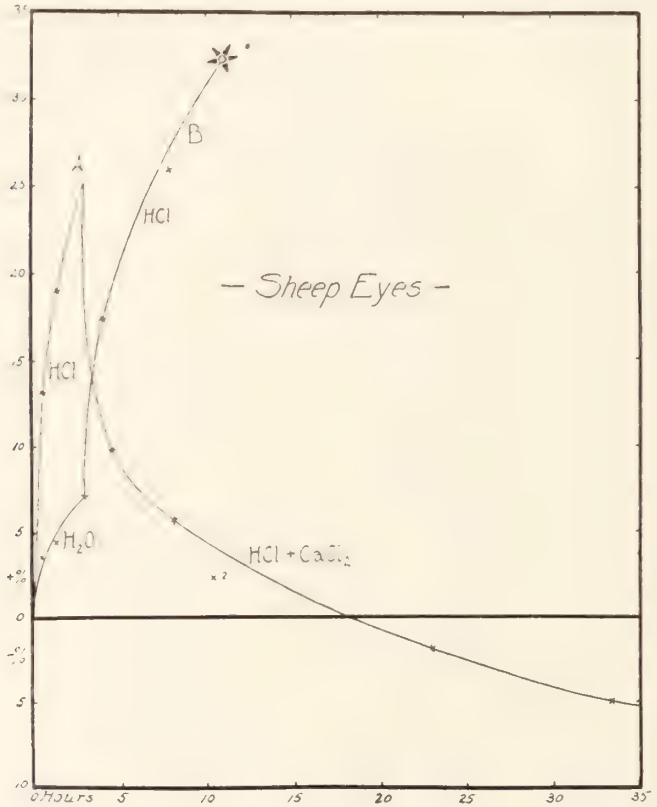


FIGURE 43

eye bursts. Let it be mentioned in conclusion that the eye, also, suffers somewhat permanently from every condition through which it has passed. Once, for instance, an eye has been in an acid solution containing a salt, it does not subsequently swell as much in a pure acid solution (in the time allowed in these experiments) as it would have done had it been placed here directly.

V. THE BIOLOGICAL SIGNIFICANCE OF THE ANALOGY BETWEEN THE ABSORPTION OF WATER BY CERTAIN COLLOIDS AND THE ABSORPTION OF WATER BY MUSCLE AND THE EYE.

That the colloids of the tissues might be of some importance in determining the water content of cells has occurred to several observers, but very careful study of their papers shows that for the most part they have dismissed the thought with little more than mere reference to its possible role, or the added remark that its significance in the general problem cannot be great. Interestingly enough W. Pfeffer,[1] who worked so earnestly for the establishment of the importance of osmotic pressure as the great regulator of the water content of cells, seems to have been the first to regard the pressure of swelling (Quellungsdruck) as of use in explaining various exceptions to the laws of osmotic pressure as studied in botanical material. More recently Franz Hofmeister[2] has developed the same idea in his fundamental discussions of the biological significance of the colloidal state. Durig[3] has expressed the belief that studies on the swelling of colloids might help to explain the exceptions to the laws of osmotic pressure noted in his experiments on the absorption of water by frogs in various solutions. Rudolf Höber[4] and E. Overton[5] have also considered the subject. Both, however, lay greatest stress on the osmotic conception of water absorption by cells, especially as modified by the fact that the osmotic membrane about cells is supposed to be fat-like (lipoidal) in character. The role of the colloids is by both these authors not considered the fundamental factor

[1] Pflanzen Physiologie, Leipzig, 1897, i, 116; see also the first edition of 1881, i, 26–29.
[2] Archiv f. exp. Path. u. Pharm., 1891, xxviii, 210.
[3] Pflüger's Archiv, 1901, lxxxv, 401.
[4] Physikalische Chemie d. Zelle u. d. Gewebe. Zweite Auflage, Leipzig, 1906, 61, 62, and 70; see also Korànyi-Richter, Physikalische Chemie u. Medizin, Leipzig, 1907, i. 294.
[5] Nagel's Handbuch der Physiologie, Braunschweig, 1906, ii, 744, where references to his earlier papers will be found.

in absorption, but is simply pointed to as one that is useful in explaining some of the many exceptions found to exist between the actual and the theoretical behavior of cells when these are regarded as osmotic systems. Much the same position is taken by H. J. Hamburger.[1] The role of the colloids as a factor in the regulation of the water content of organs has also been discussed by Wolfgang Ostwald[2] and Wolfgang Pauli.[3] Pauli points out that the swelling of red and white blood corpuscles in solutions of a dilute acid is not unlike the swelling of certain colloids, but in his discussion of the swelling of muscle he decides against this being essentially a colloidal phenomenon because the analogy between the swelling of muscle and the swelling of certain colloids is not sufficiently close. His unfortunate conclusion is due to the fact that he compares the careful observations at hand on the swelling of gelatine with a group of inadequate observations on the swelling of muscle.

The experiments just detailed on the analogy between the absorption of water by fibrin, and the absorption of water by muscle and the eyeball constitute, so far as I know, the first attempt to establish *experimentally* not only the quantitative but the qualitative importance of the colloids of the tissues in determining the amount of water held by them. From a quantitative standpoint, we have found that (hydrophilic) emulsion colloids are readily able to absorb amounts of water which are larger than any we have to account for in protoplasm, and from a qualitative standpoint, we have found that the behavior of protoplasm toward various external conditions, so far as its water content is concerned, is no different from the behavior of some simple colloids toward the same external conditions. But to accept the absorption of water by colloids as the most important factor in the absorption of water by the tissues, is to arraign all the explanations which have thus far been given for the normal and abnormal variations in the amount of water held by protoplasm. We

[1] Osmotischer Druck und Ionenlehre, Weisbaden, 1902–04; see especially iii, 4 to 33, 50 to 54, and 108 to 144.

[2] Personal communication.

[3] Ergebnisse der Physiologie, 1907, vi, 126 to 129.

must, in consequence, study them for a moment in order to see if the conception of the variable affinity of the colloids for water which we have introduced, merely adds to the forces already considered as active in protoplasm or whether the acceptance of the ideas here advanced necessitates a revision of our former beliefs.

We can at once dismiss as purposeless all "explanations" which are of a "vitalistic," "neovitalistic," or "physiological" character they are mere salves for the undiagnosticated sore. Of clearly defined physical or physico-chemical explanations, two have assumed special prominence. The first of these we will call, for short, the pressure theory; the second, the osmotic theory of water absorption. With the latter, we will consider that modification of it which has come with the belief that the semi-permeable membrane assumed to surround cells may be fat-like (lipoidal) in character.

1. In what has been called the *pressure theory*, variations in the pressure of circulating liquids (such as the blood or lymph) are looked upon as chiefly responsible for the variations in the amount of water held by the tissues, in that through changes in pressure the circulating liquids are supposed to be forced through the vessel walls. It is not strange that this belief should have originated and seemed especially acceptable to those biological workers whose interest centres particularly in animals which possess the conspicuous feature of a circulatory system. But the very school which laid originally most stress upon this force—the school of pathologists and the earlier physiologists—has found its efforts to increase the amount of water held by tissues through an increase by experimental means of the blood and lymph pressures, to result in failure. We need not here again point out the still more fatal argument against the pressure theory contained in the observations which show that enormous amounts of water may be absorbed in the entire absence of a circulation—a muscle absorbing more than twice its weight of water in a dilute acid, and a beef eye, enough to rupture the enormously thick and

tough sclera. The forces displayed here are so great that they cannot even be approximated by simple blood pressure. With these remarks we will temporarily dismiss the subject, for we will have to return to it later.

2. It is not strange after what has been said that the best contribution toward a physico-chemical analysis of the forces active in the absorption and secretion of water by living cells has really come through the plant physiologists. As no circulatory system at all similar to that found in the higher animals exists in plants, the plant physiologists were not led into wrong paths, and so early sought the explanation of the variable amounts of water held by tissues in the tissues themselves. As a result of the patient labors particularly of W. Pfeffer and Hugo de Vries, the conception that plant cells are surrounded by a membrane permeable to water but impermeable to substances dissolved in the water, received much experimental support. According to this *osmotic theory* the cells absorb or give off water to a surrounding medium, simply as this happens to have an osmotic pressure that is lower or higher than that existing within the cell. If the osmotic pressure within the cell is higher than that without, water passes into the cell until the osmotic concentration of the fluid contents within the semipermeable membrane is equal to that of the fluid without; or if the osmotic pressure within the cell is lower than that of the fluid without, water passes out of the cell through the semipermeable membrane until osmotic equilibrium is established on both sides of the membrane.

In the late nineties of the last century this osmotic conception of the absorption and secretion of water by cells began to find acceptance at the hands of certain animal physiologists. The names of Hedin, Hamburger, Gryns, Höber, Koeppe, stand out prominently in this work. But with improvement in methods and an increase in the number of experimental data the laws of van't Hoff as formulated for osmotic pressure were found to hold less and less closely for the phenomena observed in living matter.

We need not review in detail the arguments which have been

brought against the osmotic conception of water absorption by cells. To make the laws of osmotic pressure tenable for an animal or a plant cell, a membrane impermeable to dissolved substance but permeable to the solvent (for biological purposes this means water) must exist about the cell. In none of the cells studied has such a membrane ever been found by the examining eye. What we call the morphological cell wall is admittedly in almost all cases not concerned in the osmotic activities of the cell. Usually the layer of protoplasm just inside of this is considered the so important semipermeable membrane. This layer in plants differs in appearance from the rest of the cell protoplasm no more than the outermost edge of a leukocyte or an erythrocyte differs from the rest of the cell body. But in spite of this negative morphological finding, such a semipermeable membrane might still exist. Such a supposition, however, encounters trouble as soon as the fact is recalled that when the contents of cells are squeezed out into a solution these cell fragments (which assume a spherical shape) behave just as the uninjured cell did before. This observation, which it seems to me points decidedly against the existence of semipermeable membranes, has been accounted for by saying that the fragments form a new semipermeable membrane about them as soon as they come in contact with the solution into which they are dropped—supposedly in much the same way as new precipitation membranes may be formed in physico-chemical experiments. But in physical chemistry this formation of new precipitation membranes is not so universal an affair; it occurs only when two so-called membrane forming solutions are brought in contact with each other, and it is hard to conceive of protoplasm being able to form a semipermeable membrane with just any solution with which it is brought in contact. The attempt may be made to meet this objection by saying that it is the universally present fat-like constituents (the lipoids) of the tissues which go to form the membrane when the cell fragments are dropped into any watery solution, but as we shall soon see, the permeability of the lipoids to dissolved substances is far too limited to help us much toward an understanding of the phenomena that we are discussing.

Yet other arguments can be brought against this belief in the existence of semipermeable membranes about cells. We simply do not know of one animal or vegetable cell that satisfies the demand of being impermeable to all dissolved substances contained within the cell protoplasm or dissolved in any medium surrounding the cell. The conception of such a cell is, in fact, impossible; for how could such a living cell rid itself of its useless metabolic products, or gain necessary ones from the outside? Both processes are absolutely indispensable for the continuation of life. To meet these arguments the membranes about cells have been assumed to be permeable to some substances and impermeable to others. An enormous literature has sprung up regarding this partial permeability of cell membranes, but even this meets with difficulties, for there is so little apparent connection between the kind of substances that are exceptions to these laws of osmotic pressure. Only the members of one group—that which has a ready solubility in the fats—have been recognized as having one property in common, and to account for their entrance into cells, the osmotic membrane about cells has been endowed with lipoidal characteristics. The unfortunate part about this theory, which in essence is that of Overton, is that while it renders easier our understanding of the absorption of these lipoid-soluble substances, it makes it impossible for the salts to enter most cells. Overton has, in fact, come to such a conclusion, which cannot, however, be right, for the modifications that we can induce in the physiological reactions of various tissues through different electrolytes indicate very clearly that these *must* be able to enter the cells. We shall return to this question later.

The argument against the osmotic conception of water secretion and absorption by the cell is not finished with these remarks regarding the semipermeable membrane itself. If the cells obey the laws of osmotic pressure, then it is demanded that in solutions of different substances having the same osmotic pressure the volume of the cells shall be the same. Exceptions to this conclusion are the *rule* with cells. This has been proved with red

blood corpuscles and is most evident in experiments with muscle. In isosmotic solutions of different salts, frog's muscle absorbs very different amounts of water, as is shown by the experiments of Loeb, Webster, Overton, and my own as described in this paper. Again, if the laws of osmotic pressure are tenable for cells, then every increase in the concentration of the medium surrounding a cell ought to be followed by a proportionate decrease in the volume of the cell. As a matter of fact, Koeppe found that red blood corpuscles always shrink *less* than is expected when the concentration of the surrounding medium is raised. The same fact is to be observed in experiments on muscle, living frogs (Durig), enucleated eyes, and the ligated legs of frogs.

All these facts indicate very clearly that there is little reason for accepting the osmotic theory as of paramount or even great importance in the explanation of the ways and means by which tissues absorb or secrete water. I would like to be correctly understood in this matter. I am not maintaining that the laws of osmotic pressure *may* not account for *some* of the phenomena observed in at least *some* cells. This is a question which on the basis of the experimental data now available cannot be decided, but the biological significance originally attributed to these laws has certainly been much overrated. Nor does such a decision against the role of osmotic pressure in these biological phenomena minimize in the slightest the value of the work of that score of investigators who have busied themselves with this problem—they have made not only the best effort to analyze physico-chemically the forces active in the absorption and secretion of water by the cell and its myriad associated problems, but they have laid down the experimental data upon which all subsequent workers upon this problem must build.

3. Before passing to the discussion of Overton's attempt to account for some of the exceptions to the validity of the laws of osmotic pressure in these cellular phenomena, let us see what sort of a substitute for, or addition to, our present conceptions regarding the forces active in these processes is made by the ideas

regarding the role of the (hydrophilic) emulsion colloids of the tissues as advanced in the previous sections of this paper. *In this conception of the role of the colloids as determinants of the amount of water held by the tissues, we have no need for membranes.* We can dispense with them in considering the absorption and the secretion of water by cells just as we can when we consider the absorption and secretion of water by powdered fibrin or by gelatine. We are not surprised when we find that fragments of cells behave toward external conditions just as did the intact cell; in fact, we expect this behavior, for colloids constitute the body of the cell, and just in so far as the colloids in the different parts of the cell do not differ from each other, in so far also do we not expect the processes of absorption and secretion in these various parts to differ. The absence of a visible membrane does not annoy us—it simply speaks in favor of the homogeneousness of the protoplasm. The presence of any visible (not simply "osmotic") membrane (such as a cell wall) interests us much more. It introduces the factor of another kind of colloid, and with it all the possibilities arising therefrom, for all colloids, so far as water absorption is concerned, do not necessarily react in the same way either quantitatively or qualitatively toward any given set of external conditions. For this reason the protoplasm of a plant cell shrinks away from the surrounding cellulose wall when immersed in a too concentrated salt solution, and is limited in its subsequent expansion if removed to water. The possibility of explaining the whole problem of inequalities in the amount of water held by *different parts* of the *same cell* (including the much neglected intercellular substances), therefore, evidences itself here.

What holds for the single cell holds also for *different cells*, in consequence of which we are not surprised when with differences in the colloidal constitution of different cells we find a corresponding difference in their behavior when subjected to the same set of external conditions. In œdema, for example, neighboring but morphologically different cells may show a most unequal degree of swelling. Whether we deal with different parts of the same cell or with different cells does not matter, we need no

semipermeable or other kind of membrane to render effective the absorptive powers of the (hydrophilic) emulsion colloids. As a last word, let it be added that we are now able to explain the variations in the water content of the *intercellular substances*. In the discussion of the absorption of water by the cells, these have all too often been overlooked, and this in spite of the fact that some of the grossest pathological conditions are at times limited to the very tissues in which cells are fewest, and intercellular substance most conspicuous. We need only to recall the intense œdemas of the connective tissues, and the pathological changes characteristic of myxœdema.

Two groups of substances have always stood out prominently as exceptions to the laws of osmotic pressure as considered active in protoplasm, the acids and the alkalies. The various tissue elements which have been examined in dilute solutions of these substances—red and white blood corpuscles, muscle, kidney, and liver cells—all show an absorption of water which is vastly greater than can be accounted for on the basis of any idea of osmotic pressure. In fact the amount that muscle can swell in dilute acids has been employed by Overton as a powerful argument against the ordinary osmotic conception of absorption in general. He has shown very clearly that were all the proteins, carbohydrates, and fats contained in muscle split into their simplest products, a sufficient yield of molecules and ions would not be obtained to furnish an osmotic pressure adequate to account for the amount of water absorbed. We have no trouble in accounting for this behavior of the acids and alkalies on the basis of our colloidal conceptions. The acids and the alkalies are the substances most capable of altering the affinity of the hydrophilic colloids for water. The observation of Hamburger, that the volume of red blood corpuscles and the diameter of white blood corpuscles increases progressively with every increase in the concentration of the acid or the alkali in the solutions surrounding them, finds a ready explanation in the facts outlined regarding the swelling of fibrin and gelatine.

We have also no difficulty in accounting for the unequal swell-

ing of cells in osmotically equivalent solutions. We have found the same to be true of the swelling of fibrin and gelatine. We have been able to go even farther: we have found that the same group of substances which have proved exceptions in the osmotic studies on cells, also show a like exceptional behavior when we deal with fibrin.

To find an analogue for the failure of muscle, red blood corpuscles, and cells in general to shrink the calculated amount with every unit increase in the concentration of the added salt is also simple. We need only to refer once more to the experiments on the swelling of fibrin and of gelatine in which we found that here, too, doubling the concentration does not halve the volume—the amount of decrease is always less than anticipated.

4. Briefly stated, Overton assumes that the surface of cells is made up of a substance which in its properties as a solvent is not unlike ether or the fatty oils. He was led to this conclusion in his attempt to account for the fact that a great many substances when dissolved in water are unable to plasmolyse cells. For example, while the various salts, at a suitable concentration, lead to a shrinkage of the protoplasm of plant cells, a large number of other chemical compounds, such as urea, glycerine, various sugars and alcohols do not do so. According to the osmotic theory, the membranes assumed to exist about cells are said to be permeable to this group of substances. Overton has shown that all these substances have the property in common of being soluble in fats and fat-like bodies, and as these are universally present in protoplasm (as the lipoids -lecithin, cholesterin, protagon, cerebrin), he has tried to account for the permeability of cells to these substances by saying they go through these cell membranes because they are soluble in them. Most salts do not go through because they are insoluble in this surface film, in consequence of which they may extract water from the cell and so lead, at the right concentration, to its plasmolysis.

The great difficulty with Overton's explanation is that in accounting for the entrance of the lipoid-soluble substances, he

makes it impossible to explain the entrance of the much larger group of substances of which the acids, alkalies, and the salts are representatives, the vast majority of which are not soluble in fat-like bodies. But judging from physiological experiments, we know that these *must* be able to enter cells, otherwise how could we account for the marked variations we are able to produce in the reactions of protoplasm by means of these very substances. It is not enough to say that these salts move only through the intercellular substances. That certain salts in certain tissues *may* move more easily through the intercellular substance than through the cells themselves is not questioned—salts do not diffuse with the same ease through different colloids—but that does not alter the main contention that salts can and do pass into the cells themselves.

Again, the assumption that cells are surrounded by a fat-like membrane makes it impossible to account for the entrance or exit of *water* from the cell. Water is not soluble in the fats (except theoretically), and hence cannot pass through a layer of it, and yet we know that within exceedingly short intervals of time cells are capable of absorbing or secreting enormous amounts of water. The attempt might be made to explain this absorption of water by calling attention to the colloidal properties of at least some of the lipoids—lecithin, for example, which is capable of absorbing water when dropped into it (Höber). But as soon as we accept this as true then our reasons for the non-entrance of the salts fall away, for when a lipoid absorbs water it loses at the same time its property of being a solvent only for the lipoid soluble substances.

What, finally, do we attain when the lipoid soluble substances have penetrated the lipoidal surface membrane? We accomplish only an accumulation of the absorbed substance within the membrane itself, and just inside of this. We have not yet explained how it gets through the rest of the cell.

In the attempt to harmonize these conflicting notions, Nathansohn[1] has assumed the surface of cells to represent a sort of mosaic,

[1] Pringheim's Jahrbücher, 1904, xxxix, 607. An excellent review is found in Höber: Physikalische Chemie d. Zelle u. d. Gewebe, Zweite Auflage, Leipzig, 1906, 176.

a part of which is formed by the fat-like substances, another part of protoplasmic material possessed of the properties of a semipermeable membrane. This "protoplasmic material" must be made up of the protein constituents of the cell, though the (colloidal) carbohydrate constituents may play, at least qualitatively, an equally important role. The objections that must be raised against Nathansohn's conception are clearly a combination of those that have formerly been raised against the osmotic conception alone, plus those that can be lodged against Overton's ideas.

For the reasons already detailed I object to this belief in membranes about cells. Their existence is purely an assumption—has never been proved experimentally, and there exists decided evidence against their presence. The conception of Nathansohn is, however, valuable because it brings out the idea of a mixture in protoplasm of substances having fat-like characteristics with such as do not possess this property. But to confine this mixture to the surface of cells is wrong—it is too limited. *We will encounter no difficulty in explaining the various experimental facts at our disposal by ignoring altogether the existence of impermeable or partially permeable cell membranes and simply remembering that the substance of a cell consists of a mixture of different colloids. A part of these are colloidal solutions of the proteins with physical and chemical properties analogous to the physical and chemical properties of fibrin, gelatine, etc.; a part, colloidal solutions of the lipoids, which while sharing some of the properties possessed by the protein colloidal solutions, such as their power of swelling in water, have specific properties of their own, such as their power of taking up substances soluble only in the fat-like bodies.*[1]

In order to complete my argument let me add at once that *we cannot and must not consider the absorption, or secretion, of water and the absorption, or secretion, of a substance dissolved in the water as identical processes.* Workers in biology make this mis-

[1] The role of the colloidal *carbohydrates* is ignored in this discussion simply because very little of immediate interest to us has as yet been done with them.

take constantly. The processes of the absorption of water and the absorption of dissolved substances do not parallel each other in simple physico-chemical experiments, and so need not, and do not, in living cells. The two are frequently *associated*, and may at times lie so closely together that they give the impression of running parallel with each other.

The absorption of water by the tissues I have attributed primarily to the state of the (hydrophilic) emulsion colloids. The colloidal proteins undoubtedly appropriate the lion's share in this phenomenon, but the colloidal lipoids and the colloidal carbohydrates, in so far as they have an affinity for water, and it is governed by laws similar to those that govern the absorption of water by such substances as fibrin and gelatin, must not be ignored.

So far as the absorption of *dissolved substances* is concerned, it is quite independent of the amount of water absorbed (except as the absorbed water retains the characteristics of ordinary water and so increases the bulk of solvent for water-soluble substances in the cell). Inasmuch as this paper deals with the absorption of water, a detailed discussion of this absorption of dissolved substances is out of place. But the two processes overlap each other so frequently that attention may well be directed to the excellent service that is and will be rendered the problem by *the laws of simple solution, of adsorption, and of partition* in untangling the maze of phenomena encountered under the general caption of absorption by living cells.

It seems possible that in some cells and with some dissolved substances the concentration of the dissolved substance in the surrounding medium and in the cell ultimately gets to be the same in both. This has its parallel in the ultimate uniform distribution of the dissolved particles of a substance (say copper sulphate) throughout a solution in which the dissolved substance was at first not uniformly distributed. If instead of letting such a salt diffuse into the pure solvent we approximate biological conditions by letting it diffuse into a colloidal mass (gelatine, for example) the salt may ultimately again be equally concentrated within and without the colloid (Franz Hofmeister). Depending

upon the colloid and the nature of the dissolved substance, this need not, however, be the case—the dissolved substance may in the end be present in either a greater or a less concentration in the colloidal mass than in the surrounding medium. This has a familiar parallel in both vegetable and animal cells. Such differences between the concentration of dissolved substance in the colloidal mass and in the surrounding medium become particularly marked if instead of a crystalloid, a colloid makes up the "dissolved" substance. Under such circumstances the phenomena of *adsorption*, which while present in the case of the crystalloids, become particularly prominent. The *law of partition* becomes prominent as soon as the dissolved substance is either more or less soluble in some substance contained within the cell than in the solvent surrounding the cell. Hence the special case and rapidity of absorption of substances readily soluble in fat-like bodies (lipoid-soluble substances) by cells containing such lipoids. In this enormous difference between the solubility of substances in water and in the fat-like bodies, both as to rate of solution and absolute amounts dissolved (coefficient of partition), we can find the explanation not only of the rapidity with which the lipoid-soluble substances enter cells, but also of the large amounts that may be absorbed.

When we consider protoplasm simply as a mixture of different colloids (proteins, fats, carbohydrates), and consider the special characteristics of absorption that arise out of such a mixture not only as regards water, but as regards substances dissolved, or pseudo-dissolved (colloids) in it, it seems to me that we can account without difficulty, even without membranes, for all those phenomena which have up to the present been interpreted through the assumption of semipermeable, partially permeable, and lipoidal membranes about cells.

VI. ON THE NATURE AND THE CAUSE OF ŒDEMA.

We are in a position now to return to our problem of œdema and to attempt an analysis of its nature and cause. Our experi-

mental study of the subject thus far has led to the conclusion that *the cause of œdema resides in the tissues.* But what changes do the tissues suffer in order to get into this pathological state? In order to render clear the argument that follows and the purpose of each experiment, we will at once state our conclusion. *A state of œdema is induced whenever, in the presence of an adequate supply of water, the affinity of the colloids of the tissues for water is increased above that which we are pleased to call normal. The accumulation of acids within the tissues brought about either through their abnormal production, or through the inadequate removal of such as some consider normally produced in the tissues, is chiefly responsible for this increase in the affinity of the colloids for water, though the possibility of explaining at least some of the increased affinity for water through the production or accumulation of substances which affect the colloids in a way similar to acids or through the conversion of colloids having but little affinity for water into such as have a greater affinity must also be borne in mind.*

Our proof for the truth of this contention will take three directions:

1. An abnormal production or accumulation of acids, or conditions predisposing thereto, exist in all states in which we encounter the development of an œdema.

2. The development of an œdema in tissues is antagonized by the same substances which decrease the affinity of the (hydrophilic) emulsion colloids for water (salts) and is unaffected by the presence of substances which do not do this (non-electrolytes).

3. Any chemical means by which we render possible the abnormal production or accumulation of acids in the tissues is accompanied by an œdema.

We will now consider each one of these separately:

1.

We are especially prone to see states of œdema develop in conjunction with *circulatory disturbances.* Whether these be purely local in character, induced perhaps through thrombosis,

embolism, or ligature of an artery or a vein, or more general, as when the heart is diseased, we note at all times the development of an œdema, which, generally speaking, is proportional to the severity of the interference with the circulation. If a good collateral circulation exists, the thrombosis, embolism, or ligature may be entirely without effect, or if such a collateral circulation is gradually established the œdema may gradually pass away; but if neither of these is possible, then the œdema may exist for a very long time, and the circulatory disturbance ultimately lead to the death of the part.

When, on the other hand, the œdema has a more general cause, as a valvular defect in the heart, then we are able to alleviate this œdema just in so far as we are able to increase the blood supply to the œdematous organs, and prevent conditions of lack of oxygen developing in these organs (as through exercise of the muscle, for example). Through restriction of those physiological functions which we know normally to be followed by an increased demand for blood (rest in bed) and the use of methods which make for a more efficient heart activity (postural changes, digitalis) we can therefore benefit our patient. These simple clinical facts are usually interpreted by saying that the œdema develops through the blood stasis, wherewith is associated an increased capillary blood pressure and serum is squeezed into the surrounding tissues. And yet in these very clinical experiences lies a simple proof that this interpretation cannot be correct, for digitalis, which improves the patient's condition, does not *decrease* the blood pressure to which we have attributed a role in the production of this œdema, but further *increases* it.

We will have no difficulty in interpreting the variations in the severity of a local or a general œdema due to a circulatory disturbance when we say that *every condition that makes for a state of lack of oxygen in the œdematous parts, be this through disturbances in the affected parts themselves, or in some distant organ, as the heart, makes for an increase in the severity of the œdema.* This brings us face to face with the following question: Is every state of lack of oxygen accompanied by an abnormal

production or accumulation of acid? for, as already stated, this is what we need and know from our previous experiments to be most potent in increasing the affinity of the tissue colloids for water.

To answer this question we will introduce the striking experimental findings of Trasaburo Araki.[1] This author has shown that *in lack of oxygen, no matter how produced, dogs, rabbits, and frogs excrete lactic acid in their urine* in addition to various other abnormal substances. Under ordinary circumstances this lactic acid is not to be found in the renal secretions, but let the oxygen supply to these animals be sufficiently interfered with, by any means whatsoever (through confinement in a closed box, through carbon monoxide poisoning, or through the injection of curare, morphine, amyl nitrite, or cocaine), and the acid appears. Lest the objection be raised that these remarks may hold for various animals, but need not necessarily be true for human beings, let it be noted that Araki found lactic acid in the urine of epileptics voided shortly after their seizures. As a proof that lactic acid is not necessarily the only acid that may be or is produced in states of lack of oxygen, we can mention E. Mendel's[2] finding that the phosphoric acid content of the urine is increased immediately after epileptic seizures and in apoplexy. We may also call to mind Hoppe-Seyler's analysis of various œdema fluids which he found to contain, besides lactic acid, valerianic, succinic, and butyric acids.

The lactic acid found in conditions associated with a lack of oxygen *is produced in the tissues*, enters the blood, and is excreted by the kidneys. This has been proved by Araki's later publications and through Hermann Zillessen's[3] experiments. Zillessen found that when the oxygen supply to a muscle or the liver is shut off for a variable number of hours through ligature of the arteries supplying these parts, an increased production of lactic

[1] Zeitschr. f. physiol. Chemie, 1891, xv, 335 and 546; ibid., 1894, xix, 422; see also Hoppe-Seyler, ibid., 1894, xix, 476.

[2] Archiv f. Psychiatrie u. Nervenkrankheiten, iii, 636.

[3] Zeitschr. f. physiol. Chemie, 1891, xv, 387.

acid occurs. If the ligature is loosened and the first blood returning from the oxygen-starved tissues is analyzed, this is found to be particularly rich in lactic acid, and if the blood is titrated, it is found to have a diminished capacity for neutralizing a standard oxalic acid solution.[1] Zillessen was also able to demonstrate the production of lactic acid in animals poisoned with hydrocyanic acid, which we know from Geppert's studies to owe its action to its power of inducing a state of lack of oxygen in the tissues.

The accumulation of carbon dioxide in the tissues is also of importance. The ordinary circulatory disturbances while making for a decreased supply of oxygen to the tissues also make for an accumulation of carbon dioxide. In experiments with fibrin which I placed in distilled water in ordinary "soda" bottles, and then had charged with carbon dioxide at various pressures in a local mineral water establishment, I found a marked increase in the amount of the swelling with every increase in the concentration of the carbon dioxide. The observation of Strassburg and Ewald, that the carbon dioxide content of œdema fluids and of tissues deprived of a circulation runs very high, is therefore not to be disregarded in trying to find a cause for the increased affinity of the tissues for water in a state of disturbed circulation.

In place of an interference with the local blood supply, or a disturbance of the general circulation due to an inadequately functionating heart, the lack of oxygen in the tissues which we look upon as the predisposing cause to the œdema may be brought about by other means. Any interference with the normal oxygen carrying power of the blood may therefore be expected to induce a state of lack of oxygen in the tissues. We find in this a ready explanation of the œdemas so frequently noted in a severe *anæmia*, no matter what its cause may be. It is of interest, therefore, that Felix Hoppe-Seyler[2] was able to isolate lactic acid from the urine in two cases of severe anæmia. As additional evidence

[1] Araki, Zillessen, and most of the older observers speak of a "decreased alkalinity" of the blood. Since modern physico-chemical measurements have shown the blood to be neutral in reaction, it is best to state the experimental findings of these authors as above.

[2] Zeitschr. f. physiol. Chemie, 1894, xix, 473; Araki's article.

in favor of the abnormal production of acid in the anæmias we may cite R. von Jaksch's[1] findings, amply verified by subsequent workers, that the blood shows a distinctly diminished power of neutralizing acid in *pernicious anæmia, leukæmia, and chlorosis.* That this decrease in the ability to neutralize acids really means that an abnormal production of acids has occurred in the tissues of the anæmic individual, is evident not only from the work of Araki and Zillessen already cited, but from von Jaksch's own finding that in carbon monoxide poisoning in which the abnormal presence of lactic acid in the urine has been indisputably shown by Araki, there exists also a distinct decrease in the normal capacity of the blood to neutralize acids.

An œdema, often of a severe grade, is the almost constant accompaniment of various states of *inanition.* It is observed not only in starvation, but in the various forms of scurvy that are observed clinically, and the experimental forms that may be induced in animals. What evidence have we for the abnormal production or accumulation of acids in all these conditions to account for the œdema? We are, first of all, not without clinical evidence. The observations on human beings undergoing a voluntary fast all agree in that they show the urine to grow progressively more acid with each day of starvation. The only exception to this rule was noted by Luigi Luciani[2] in his study of Succi during a thirty days' fast. For the first six days of his fasting there was a gradual increase in the acidity of the urine; for the rest of the period it remained very high in spite of the fact that he consumed large amounts of alkaline mineral water.[3] A. E. Wright[4] has made a further observation of interest. He noted a diminution in the capacity of the blood to neutralize acid in seven cases of scurvy.

[1] Klinische Diagnostik, Fünfte Auflage, Berlin, 1901, 5.

[2] Das Hungern, Hamburg und Leipzig, 1890, 164.

[3] Succi's fasting period was long enough to have allowed of the development of an œdema, and yet none is noted in Luciani's account of the case. I attribute this to the beneficent effects of the mineral water he consumed. See the effects of salts on œdematous muscles and glaucoma given below.

[4] Lancet, 1900, ii.

Much more convincing are the experimental studies on starving animals. The normally acid urine of the carnivora becomes much more intensely so with the progress of the starvation, and in herbivora, the normally alkaline urine becomes highly acid. The same occurs if animals (especially herbivora) are fed an exclusive diet of any sort. An exclusive oat diet, which is high in acid salts and low in calcium, is very quickly fatal. H. Weiske[1] found that when certain mineral salts, especially calcium salts, are added to the pure oat diet the animal fares much better. A very thorough study of starvation and such one-sided diets, rich in acids and poor in calcium, has been made by Axtel Holst and Theodor Frölich.[2] They describe as constant findings in their experiments the occurrence of œdema. "A pronounced universal anasarca" was noted in all the starved animals, while those fed exclusively on oats, barley, wheat, or some of their derivatives showed various degrees of œdema up to such universal anasarcas. Close scrutiny of Holst and Frölich's experiments would seem to indicate that the more liberal the variety of the salts in the diets, the less the tendency to observe an œdema.

We must also call attention to the work of Hildebrant,[3] who found that rabbits which had been kept upon an "acid" diet (exclusive oat diet) for a short time died rapidly when fed a few grams of dextrose. The reason for this is that such animals form oxalic acid from the dextrose. Their death can be prevented by feeding them any soluble calcium salt with their oats, or the dextrose.

Œdema is a not uncommon accompaniment of *fever*. In some fevers it constitutes a symptom so marked that it is looked for clinically; in others, the increased amount of water held by the patient is clearly indicated by his failure to secrete an amount of water through kidneys, lungs, skin, and bowels, the equivalent of the amount ingested. With remission or discontinuance of the fever there has been noted by the most careful observers an

[1] Zeitschrift f. Biologie, 1895, xxxi, 421.
[2] Journal of Hygiene, 1907, vii, 634.
[3] Zeitschrift f. Physiol. Chemie.

increase in the output of water by all the water-secreting organs above the amount ingested.

I am not maintaining, of course, that the fever, per se, is the cause of the œdema. It may contribute toward this end, however, for we observed gelatine to absorb more water at a higher temperature than at a lower one. In fevers of the most varied kinds we note a highly acid urine, and von Jaksch found a constant diminution in the neutralizing power of the blood for acids. As to the cause for this acid production we are still in the dark—it could be the indirect result of toxic degenerative changes induced in certain organs (for example, the kidneys or the heart), but it can certainly occur even without a lesion of these through the action of the poisonous (fever producing) substances upon the tissues generally. We need only call to mind the great inhibition of various oxidations occurring normally in the body and necessary for the continuation of life that various bacterial and animal toxines produce. Our classification of these œdemas is necessarily an arbitrary one, and what I have called here the œdema of fever must ultimately, no doubt, fall into the group of the general toxic œdemas.

Œdema is an almost constant symptom of *nephritis*. We cannot, of course, accept the belief that the œdema associated with diseases of the kidneys is dependent upon the increased blood pressure which is found in *some* cases of nephritis. The failure to find *any* circulatory disturbances in some of the severest cases of nephritis associated with the most intense grades of œdema itself argues against this. Pathologists and clinicians have alike to learn that this problem of nephritis has contained in it a multitude of problems each one of which most be settled by itself. No more fundamental fact regarding the kidneys is better established on experimental grounds, or more commonly ignored than that *the secretion of water by the kidneys and the secretion of the substances dissolved in it are separate processes;* that, in fact, the behavior of a kidney toward the secretion of one chemical substance is no indication of what its behavior will be toward

another. The failure to recognize this fact is in large part responsible for the endless confusion existing today in our conceptions of the cause, nature, and consequences of nephritis. (See Section IX, on the kidney.)

Can we adduce any facts to indicate that in nephritis we have conditions existing which make for an increased affinity of the tissues for water? In favor of the abnormal production or storage of acids we note the fact that the urine of nephritics is always acid in reaction, and often highly so. More convincing still to my mind is von Jaksch's finding that the "alkalinity" (acid combining power) of the blood is constantly and markedly decreased in the severer kidney inflammations. This existence of a constantly and highly acid urine, and a lowered capacity of the blood to combine with acids, may at first sight seem weak evidence in favor of the abnormal production of acids in this condition and in certain others associated with œdema that we have discussed. I admit that more definite and quantitative data would be most acceptable, and yet those at hand are entirely convincing. We need only to remember that in the severest experimental intoxications with acids, those in which large amounts of acids of known strength are introduced into the stomach, peritoneal cavity, blood, or subcutaneously, and the animal dies, no more evidence of the acid intoxication can be found than just such an increased acidity of the urine and decreased acid-capacity of the blood. Let it be further recalled that a degree of acidity to which our ordinary indicators respond only indistinctly shows itself by marked differences in the swelling of colloids.

We learn from Araki and Zillessen's observations that the production of lactic acid occurs in animals no matter how the condition of lack of oxygen is induced. In their experiments they used all kinds of methods to induce a lack of oxygen varying from those which act through direct interference with the oxygen supply to the animal (compression of trachea) to those which we know owe their effect to an action upon the oxidizing ferments of the tissues themselves (hydrocyanic acid). It is of

much interest, therefore, that A. Jolles and Oppenheim,[1] and in the United States, M. C. Winternitz and J. C. Meloy,[2] have found substances present in the blood of nephritics which interfere with at least some of the oxidation phenomena which we know are necessary for the proper continuance of life.

We can advantageously consider next what may be called the *œdema of the dead*. After death, as is well known, the tissues rapidly become acid in reaction, so intensely so, in fact, that our commonest and coarsest indicators suffice to show its presence. For the most part the acid formed is lactic acid. It matters little what we assume to be either the origin of this acid or the exact chemical change whereby it is produced. The presence of so much acid in the tissues gives us all the conditions necessary for the development of the most intense grades of œdema. Since our conception of œdema possesses no "vitalistic" attributes, we are not surprised to find that *a dead body develops an œdema quite as readily, if not more readily, than a living one*. This explains the "œdema" which develops in the dead when they lie in water. A series of experiments which I have made with winter frogs indicate how much such dead bodies absorb. While living frogs kept up to their necks in distilled water for several days showed a variation of less than 3 per cent. in weight, the same frogs after being killed gained progressively until, at the end of sixty hours, they had absorbed from 30 to 40 per cent. their original weight.

It is self-evident that what has been said regarding the general œdemas holds also for the *local œdemas*. There is no imaginable difference between the cause for a general œdema, the result of a leaking heart valve, and the cause for the local œdema observed in an *infarcted area*, except that if the infarction is due to plugging of an end artery with an embolus, no blood pressure is available for its explanation. But this is not needed, for through the increase

[1] Münchener med. Wochenschr., 1904, xlvii, 2083.
[2] Journal of Experimental Medicine, 1908, x, 759; also Winternitz, ibid., 1909, xi, 200.

in the affinity of its colloids for water the infarcted area has no difficulty in absorbing fluid from any neighboring source—as does an amputated frog's leg or a dead body from the water in which it lies. For this reason the infarct in its earlier history always shows itself as the familiar pyramidal, somewhat swollen, firm mass which stands out prominently from the surrounding tissues. The subsequent decrease in size is due to a combination of changes (coagulation, autodigestion) whereby the affinity of the tissue colloids for water is again decreased.

The *gangrenes* present the same problem as the local circulatory disturbances. Their chief interest to us lies in whether they shall be moist or dry. If water is furnished the dead or dying tissues, either from without or through the blood or lymph circulation, they swell and a moist gangrene results; if this does not happen, we have to deal with a dry gangrene. In a gangrene due to closure of a vein, we therefore expect to have a moist gangrene; while a gangrene due to obstruction of an artery is more likely to be dry.

The *local ædemas following the bites or stings of insects* have a special interest. In quite a number of these the sting carries formic or other acids into the tissues. Here we have a direct etiological factor for the production of the local œdema. In others, poisons are injected which have a well-marked reducing power. By this means a local group of cells are placed in a state of lack of oxygen through chemical means (see paragraph 3 of this section, p. 569). It is worthy of note that to start with and during the period of greatest swelling such insect stings are white, and not until later do they become red. The increased blood flow so necessary in most explanations of these local œdemas does not occur until the œdema has begun to subside. *Instead of the blood circulation determining the ædema, the ædema determines whether the circulation shall continue through the affected part or not.*

This explanation of the nature and cause of local œdemas can be further tested. The œdematous *wheals* following bites or stings can be mimicked perfectly with a gelatine plate and a

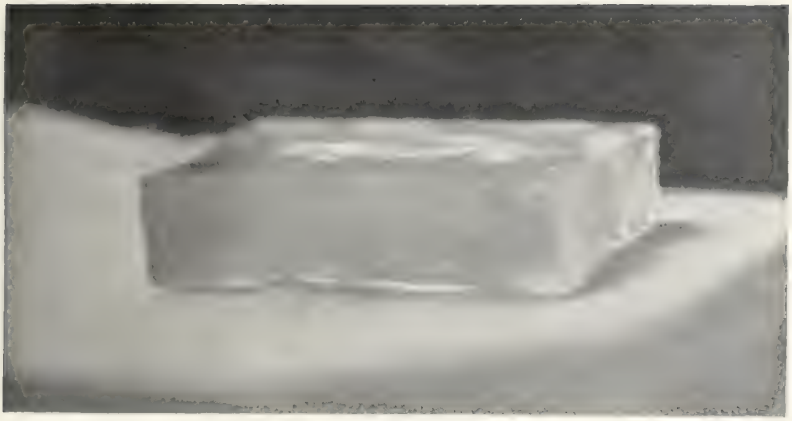


Figure 44

little acid. If with a fine hypodermic needle a little formic acid is stabbed into such a gelatine plate, and the whole is then laid into water, *an urticarial-like wheal develops about each spot pricked with the needle*, which in shape and in the rate of its development is not unlike those which follow the bite of an insect or the introduction of the formic acid laden needle into the skin.

In Figure 44 are shown some wheals which developed *accidentally* on the surface of some of my gelatine discs. The particular disc pictured had lain for thirteen days in a $\frac{1}{50}$ normal hydrochloric acid solution. The hyaline gelatine does not photograph easily, and so the figure does not indicate how clearly these wheals imitate such as are observed clinically. Those shown here are due to local infections of the gelatine with a mould. In place of the perfectly smooth surfaces such as these gelatine discs ordinarily show, we see them here studded with small mounds indicative of irregularities in the absorption of water. The cause for these local swellings may be a twofold one. As the mould developed while these discs were lying in dilute acid solutions, I question whether an additional local production of acid (of which the moulds are capable) gave rise to the local swellings. The affected spots were softer than the surrounding gelatine, and later became almost liquid. I think, in consequence, that the gelatine suffered a partial digestion under the influence of proteolytic ferments manufactured by the mould in the affected spots. Such a partially digested gelatine corresponds with the Beta-gelatine of Traube, and this we know from Wolfgang Ostwald's[1] experiments to be capable of a distinctly greater swelling than the ordinary gelatine.

In passing let it be noted that this simple observation teaches how a chemical change, in this case induced through a ferment, in the colloid itself—just such a change as might occur in living matter—may affect its affinity for water. This is a fact not without biological significance in this problem of the ways and means by which a tissue regulates its water content.

[1] Pflüger's Archiv, 1905, cix, 277.

2.

We will now turn to the second line of evidence in proof of the conception of œdema here advanced. This is intended to show that *the same conditions which have been found effective in reducing the amount of swelling of fibrin and gelatine in acid solutions counteract the development of œdema.*

In the introductory pages of this paper we became familiar with experiments which show that a circulation is unnecessary for the development of most intense grades of œdema. We found that frogs' legs which had been ligated, cut from the body, and placed in a little water, developed an œdema which mimics in every way the worst types of œdema observed clinically. We will use the œdemas developed in this way in amputated frogs' legs as material upon which to analyze the nature of the phenomenon.

(*a*) It will be well, first of all, to get some conception of the rate of water absorption (rate of development of œdema) in such frogs' (Rana) legs. Figure 45 has been introduced for this purpose. The preparations for the experiments were obtained by throwing a loose ligature about the hind legs of frogs just above the knee and amputating them, provision being made for a cuff of skin which could be pulled over the femoral stump before the ligature was finally drawn taut. In this way any leakage of absorbed water through the cut end of muscle, tendons, or bone at the point of amputation is avoided.

The steady increase in the weight of the amputated frogs' legs is readily apparent from the figure and from Table R, which contains the experimental data. The increase in weight does not go on indefinitely. It not only ceases after a time, but an actual loss of water ensues. We noted the same to be true in the experiments on muscle. The cause for this secondary drop is not yet clear. An actual loss of muscle substance through "solution" in the surrounding medium plays a partial role. I imagined that autolytic changes whereby the (hydrophilic)

emulsion muscle colloids are broken down into substances not colloidal in character might account for some of the subsequent loss. While this may play a role, experiment seems to indicate that it cannot be a great one. A series of tree-toad legs (muscles

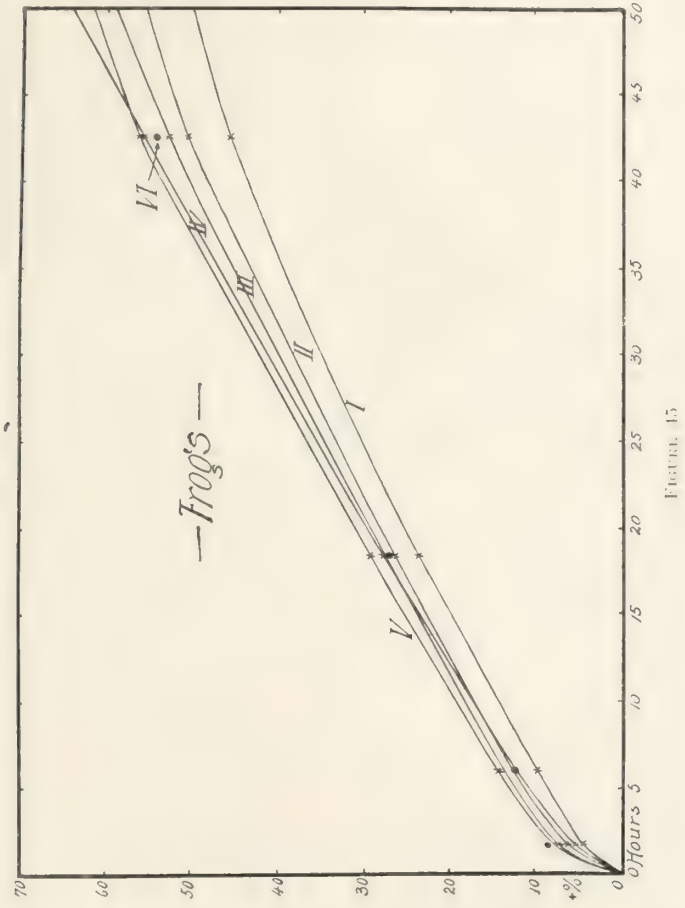


FIGURE 15

only) which I prepared aseptically and allowed to remain at body temperature in a moist chamber for various periods of time showed even at the end of a week the same absorption curve that the fresh muscle shows. I have come to conclude, in consequence, that the secondary loss of water occurs after the acid

formed in the muscle has reached a certain concentration, or has acted upon the tissue colloids for a certain length of time, or both, and that the loss of water is associated with a change in the colloids whereby these are changed from such as have

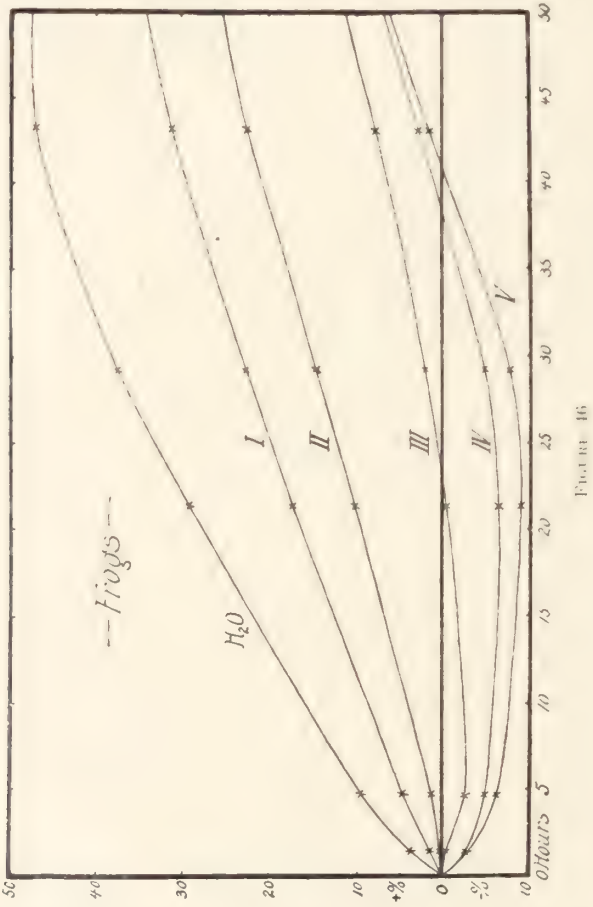


FIGURE 16

(hydrophilic) emulsion characteristics into such as have (hydrophobic) suspension characteristics. The conversion of a hydrophilic colloid into a hydrophobic one is possible physico-chemically.

Since the formation of acid in tissues deprived of a circulation is a firmly established fact—a fact which in these amputated

frogs' legs can be verified through mere application of an indicator —we have no difficulty in interpreting these experiments by saying that *the amputated frogs' legs swell in water because the affinity of their colloids is increased through the production in them of acid. The frogs' legs become ædematous for the same reason that fibrin swells more in a dilute acid than in pure water.*

(*b*) If instead of being placed in distilled water the amputated frogs' legs are dropped *into any salt solution, they swell less than in distilled water. The higher the concentration of the salt the less will the frogs' legs swell. These statements are entirely analogous to those made regarding the swelling of fibrin and gelatine in dilute acid solutions*, and are illustrated in Figures 46, 47, 48, and 49.

In Figure 46 the curves for the swelling of the amputated frogs' legs lie progressively lower with every increase in the concentration of the sodium chloride. This figure is based on the experimental findings contained in Table S.

TABLE R.—*Frogs' Legs*

Hours in the solution.	110 c.c. H_2O.	110 c.c. H_2O.	110 c.c. H_2O.
	%	%	%
0	3.66 (0)	3.34 (0)	3.01 (0)
1.45	3.84 (+ 4.9)	3.56 (+ 6.5)	3.24 (+ 7.6)
6.00	4.00 (+ 9.3)	3.77 (+12.8)	3.38 (+12.2)
18.25	4.52 (+23.4)	4.22 (+26.3)	3.83 (+27.2)
42.30	5.33 (+45.6)	5.03 (+50.6)	4.60 (+52.8)
51.45	5.52 (+50.8)	5.22 (+56.3)	4.84 (+60.8)
68.15	5.49 (+50.0)	5.34 (+59.8)	4.98 (+65.4)
76.45	5.56 (+51.9)	5.39 (+61.3)	4.86 (+61.4)
90.30	5.64 (+54.1)	5.32 (+59.3)	4.84 (+60.8)
124.45	4.96 (+35.5)	4.78 (+43.1)	4.54 (+50.8)
	(a)	(a)	(b)
	I	II	III

Hours in the solution.	110 c.c. H_2O.	110 c.c. H_2O.	110 c.c. H_2O.
	%	%	%
0	2.925 (0)	3.555 (0)	3.145 (0)
1.45	3.09 (+ 5.6)	3.82 (+ 7.4)	3.31 (+ 8.4)
6.00	3.28 (+12.1)	4.06 (+14.2)	3.53 (+12.5)
18.25	3.73 (+27.5)	4.59 (+29.1)	4.01 (+27.0)
42.30	4.55 (+55.5)	5.55 (+56.1)	4.85 (+54.2)
51.45	4.84 (+65.4)	5.76 (+62.0)	5.22 (+63.5)
68.15	5.17 (+76.7)	5.75 (+61.7)	5.54 (+76.1)
76.45	4.99 (+70.6)	5.80 (+63.1)	5.48 (+74.2)
90.30	5.00 (+70.9)	5.87 (+65.1)	5.50 (+74.9)
124.45	4.08 (+39.4)	5.17 (+45.4)	4.71 (+49.7)
	(b)	(c)	(c)
	IV	V	VI

TABLE S.—*Frogs' Legs.*

Hours in the solution.	110 c.c. H_2O.	10 c.c. 1/1 m. NaCl + 100 c.c. H_2O.	15 c.c. 1/1 m. NaCl + 95 c.c. H_2O.
	%	%	%
0	3.42 (0)	3.42 (0)	3.055 (0)
1.25	3.55 (+ 3.8)	3.48 (+ 1.7)	3.065 (+ 0.3)
4.40	3.74 (+ 9.33)	3.59 (+ 4.9)	3.09 (+ 1.1)
21.15	4.41 (+28.9)	4.02 (+17.5)	3.37 (+10.3)
29.15	4.71 (+37.7)	4.19 (+22.5)	3.52 (+15.4)
43.00	5.03 (+47.0)	4.49 (+31.2)	3.74 (+22.4)
77.15	5.00 (+46.1)	4.95 (+44.7)	4.19 (+36.1)
96.15	4.32 (+26.3)	4.83 (+41.2)	3.98 (+30.2)
	(a)	(a)	(b)
		I	II

Hours in the solution.	20 c.c. 1/1 m. NaCl + 90 c.c. H_2O.	25 c.c. 1/1 m. NaCl + 85 c.c. H_2O.	30 c.c. 1/1 m. NaCl + 80 c.c. H_2O.
	%	%	%
0	2.95 (0)	2.87 (0)	2.85 (0)
1.25	2.93 (— 0.7)	2.81 (— 2.1)	2.77 (— 2.8)
4.40	2.87 (— 2.6)	2.74 (— 4.5)	2.68 (— 5.9)
21.15	2.93 (— 0.7)	2.69 (— 6.3)	2.59 (— 9.1)
29.15	3.01 (+ 2.0)	2.73 (— 4.9)	2.63 (— 7.7)
43.00	3.18 (+ 7.7)	2.95 (+ 2.8)	2.91 (+ 2.1)
77.15	3.63 (+26.0)	3.49 (+21.6)	3.53 (+23.8)
96.15	3.36 (+14.2)	3.53 (+23.0)	3.50 (+22.8)
	(b)	(c)	(c)
	III	IV	V

(c) *When the effect of equimolecular salt solutions on the swelling of amputated frogs' legs is compared, it is found that some allow a greater swelling than others.* This is clearly shown in Figures 47, 48, and 49.

The action of a series of chlorides is shown in Figure 47. We have no difficulty in recognizing the following general grouping of the *kations* in which that least effective in preventing the swelling of the leg is placed first:

Lithium

Sodium
Ammonium
Potassium

Calcium
Barium
Magnesium
Strontium

Copper (ic)
Iron (ic)

While the exact arrangement of these kations is slightly different, *their general grouping is identical with that given for the effect*

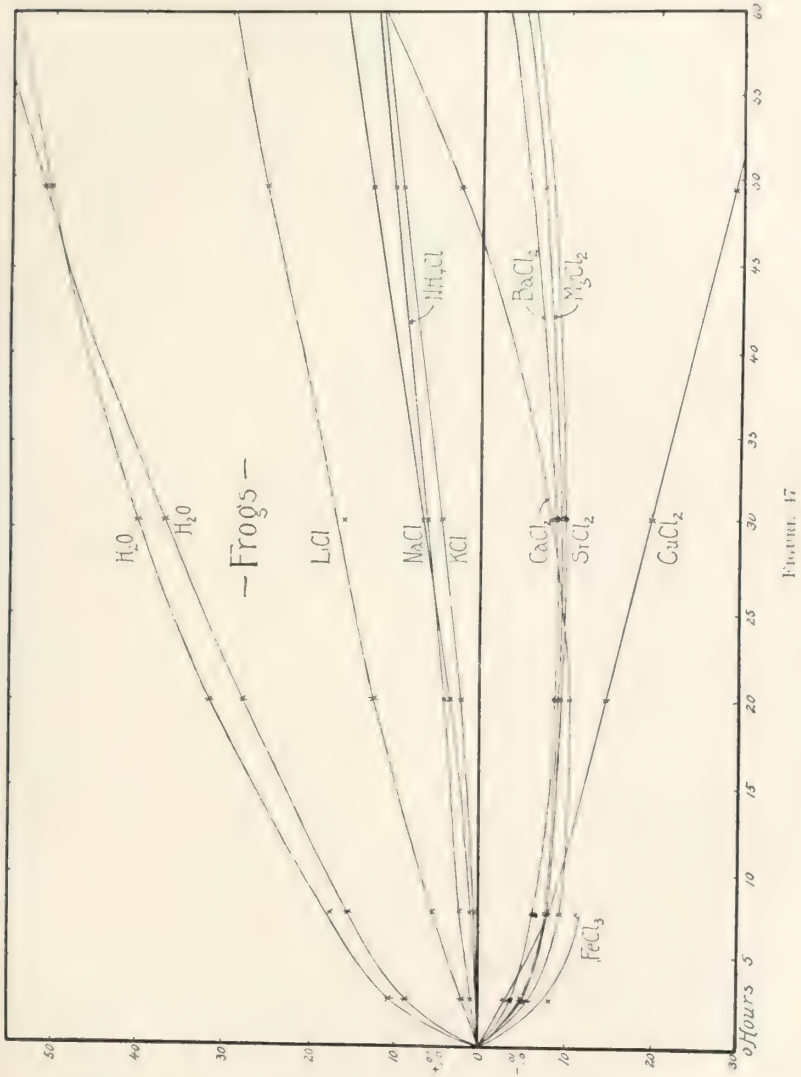
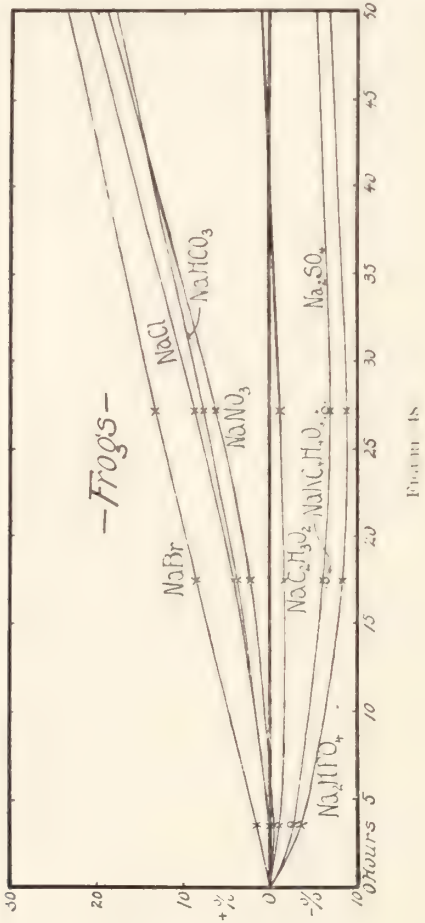


FIGURE 17

of these ions on the swelling of fibrin (also gelatine, muscle, and eyes) in acid solutions.

Figure 48 allows the comparison of a number of sodium salts. We have no difficulty in recognizing the difference in the activity



of the various *anions* which arrange themselves in the following order, that least effective in preventing the swelling being placed first:

Bromide
Chloride
Bicarbonate
Nitrate
Acetate
Sulphate
Tartrate
Phosphate

The order is practically identical with that given for the relative effect of different anions on the swelling of fibrin in the presence of an acid.

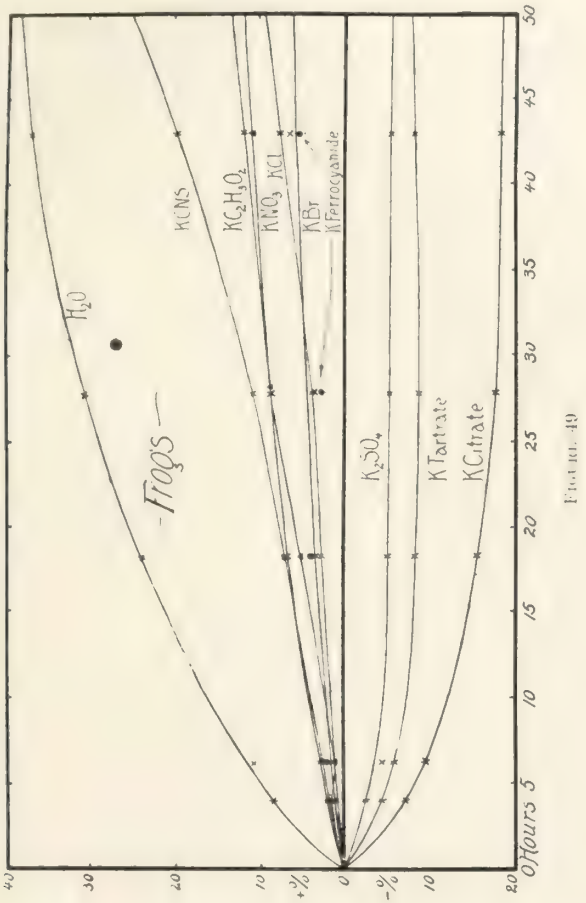


Figure 49

Figure 49 shows the curves obtained with a series of potassium salts. The acetate and nitrate curves lie somewhat high. Otherwise the order of the ions is the same as already given for the sodium salts. Of much interest is the great inhibition in swelling induced by the citrate solution, in which the frog's leg loses in weight most heavily.

TABLE T. *Frogs' Legs.*

Hours in the solution.	110 c.c. H_2O.	15 c.c. 1/1 m. ammonium chloride +95 c.c. H_2O.	15 c.c. 1/1 m. barium chloride +95 c.c. H_2O.	15 c.c. 1/1 m. cupric chloride +95 c.c. H_2O.	15 c.c. 1/1 m. ferric chloride +95 c.c. H_2O.	15 c.c. 1/1 m. calcium chloride +95 c.c. H_2O.
	%	%	%	%	%	%
0	2.45 (0)	2.38 (0)	2.91 (0)	2.82 (0)	3.59 (0)	2.70 (0)
2.35	2.71 (+10.9)	2.40 (+ 0.8)	2.71 (— 4.8)	2.73 (— 3.2)	3.30 (— 8.0)	2.54 (— 5.7)
7.35	2.87 (+17.4)	2.43 (+ 2.3)	2.68 (—7.7)	2.60 (— 7.8)	3.18 (—11.4)	2.45 (— 9.2)
20.00	3.22 (+31.6)	2.48 (+ 4.4)	2.65 (—8.6)	2.40 (—15.0)	. . . . .	2.43 (—10.0)
30.25	3.44 (+40.4)	2.52 (+ 6.1)	2.65 (—8.6)	2.26 (—19.8)	. . . . .	2.48 (— 8.1)
49.30	3.78 (+50.2)	2.64 (+11.2)	2.75 (—5.5)	2.00 (—29.2)	. . . . .	2.77 (+ 2.5)

Hours in the solution.	15 c.c. 1/1 m. lithium chloride +95 c.c. H_2O.	15 c.c. 1/1 m. magnesium chloride +95 c.c. H_2O.	15 c.c. 1/1 m. potassium chloride +95 c.c. H_2O.	15 c.c. 1/1 m. sodium chloride +95 c.c. H_2O.	15 c.c. 1/1 m. strontium chloride +95 c.c. H_2O.	110 c.c. H_2O.
	%	%	%	%	%	%
0	3.24 (0)	3.29 (0)	4.05 (0)	4.04 (0)	4.50 (0)	4.23 (0)
2.35	3.31 (+ 1.9)	3.18 (—3.3)	4.05 (0)	4.04 (0)	4.27 (—5.2)	4.61 (+ 8.8)
7.35	3.43 (+ 5.6)	3.08 (—6.4)	4.07 (+0.5)	4.07 (+ 0.7)	4.20 (—6.6)	4.88 (+15.2)
20.00	3.65 (+12.4)	3.01 (—8.5)	4.14 (+2.2)	4.18 (+ 3.4)	4.10 (—9.4)	5.41 (+27.7)
30.25	3.77 (+16.1)	2.98 (— 9.4)	4.22 (+4.2)	4.29 (+ 6.2)	4.06 (— 9.9)	5.79 (+36.1)
49.30	4.04 (+24.4)	3.04 (— 7.3)	4.44 (+9.1)	4.56 (+12.8)	4.14 (— 8.2)	6.39 (+51.0)

The experimental data from which Figures 47, 48, and 49 are constructed are contained in Tables T, U, and V.

TABLE U.—*Frogs' Legs.*

Hours in the solution.	15 c.c. 1/1 m. sodium acetate +95 c.c. H_2O.	15 c.c. 1/1 m. sodium bromide +95 c.c. H_2O.	15 c.c. 1/1 m. sodium bicarbonate +95 c.c. H_2O.	15 c.c. 1/1 m. sodium chloride +95 c.c. H_2O.
	%	%	%	%
0	3.39 (0)	3.42 (0)	3.33 (0)	3.25 (0)
3.35	3.36 (—1.0)	3.47 (+ 1.4)	3.33 (0)	3.25 (0)
17.30	3.34 (—1.6)	3.71 (+ 8.4)	3.45 (+ 3.6)	3.37 (+ 3.7)
27.15	3.36 (—1.0)	3.86 (+13.1)	3.59 (+ 7.8)	3.53 (+ 8.6)
31.45	3.43 (+1.0)	4.24 (+24.0)	3.95 (+18.6)	3.96 (+21.8)
70.35	3.55 (+4.2)	4.46 (+30.4)	4.19 (+25.8)	4.28 (+31.6)
100.55	3.66 (+7.8)	4.70 (+37.4)	4.44 (+33.3)	3.86 (+18.7)

Hours in the solution.	15 c.c. 1/1 m. sodium nitrate +95 c.c. H_2O.	15 c.c. 1/1 m. disodium hydrogen phosphate +95 c.c. H_2O.	15 c.c. 1/1 m. sodium sulphate +95 c.c. H_2O.	15 c.c. 1/1 m. sodium-potassium tartrate +95 c.c. H_2O.
	%	%	%	%
0	3.49 (0)	3.48 (0)	3.95 (0)	3.74 (0)
3.35	3.47 (— 0.5)	3.35 (—3.7)	3.84 (—2.7)	3.64 (—2.6)
17.30	3.56 (+ 2.0)	3.18 (—8.6)	3.71 (—6.0)	3.51 (—6.1)
27.15	3.70 (+ 6.0)	3.17 (—8.8)	3.67 (—7.0)	3.49 (—6.6)
31.45	4.19 (+20.0)	3.25 (—6.6)	3.74 (—5.3)	3.53 (—5.6)
70.35	4.58 (+31.0)	3.48 (0)	3.88 (—1.7)	3.58 (—4.2)
100.55	4.33 (+24.0)	3.69 (+5.9)	4.10 (+3.7)	3.73 (—0.2)

(*d*) *The addition of various non-electrolytes does not affect the amount of water that will be absorbed by amputated frogs' legs.* I have tried ethyl and methyl alcohols, urea, glycerine, dextrose, and cane sugar. The absorption of water remains practically uninfluenced in solutions of these various substances even when they are present in amounts that osmotically equal or even exceed the concentrations of the various salts which above proved so very powerful in this regard. In solutions of these non-electrolytes the absorption curves are almost identical with those given in Figure 45 for the absorption from distilled water.

TABLE V. — *Frogs' Legs.*

Hours in the solution.	110 c.c. H_2O.	15 c.c. 1·1 m. potassium acetate +95 c.c. H_2O.	15 c.c. 1·1 m. potassium bromide +95 c.c. H_2O.	15 c.c. 1/1 m. potassium chloride +95 c.c. H_2O.	15 c.c. 1·1 m. potassium citrate +95 c.c. H_2O.
	%	%	%	%	%
0	3.98 (0)	4.33 (0)	3·81 (0)	4·22 (0)	3.73 (0)
4.00	4.31 (+ 8.3)	4.42 (+ 1.9)	3·86 (+1·3)	4·25 (+0·6)	3·45 (— 7.5)
6.10	4.41 (+10.8)	4.44 (+ 2.4)	3·85 (+1.1)	4·26 (+0.8)	3·38 (— 9·5)
18.10	4.92 (+23.7)	4.61 (+ 6.4)	3·92 (+3.0)	4·31 (+2·5)	3·16 (— 15·4)
27.45	5.18 (+30.1)	4.70 (+ 8.3)	3·92 (+3.0)	4·39 (+3·9)	3·06 (—18.1)
42.50	5.44 (+36.7)	4.91 (+10.9)	4.06 (+6·56)	4·54 (+7·5)	3·05 (—18·2)
71.45	5.60 (+40.8)	5.00 (+15.4)	4.08 (+7.2)	4·57 (+8·3)	3·04 (—18.6)

Hours in the solution	30 c.c. 1/2 m. potassium ferrocyanide +80 c.c. H_2O.	30 c.c. 1·2 m. potassium sulphate +80 c.c. H_2O.	15 c.c. 1·1 m. potassium nitrate +95 c.c. H_2O.	15 c.c. 1·1 m. potassium sulphocyanate +95 c.c. H_2O	15 c.c. 1·1 m. potassium tartrate +95 c.c. H_2O.
	%	%	%	%	%
0	3.84 (0)	3.02 (0)	3.36 (0)	3·80 (0)	3·63 (0)
4.00	3.89 (+1.3)	2.96 (— 1.9)	3.40 (+ 1.1)	3·83 (+ 0·8)	3·49 (— 3·9)
6.10	3.90 (+1.5)	2.90 (—4.1)	3.39 (+ 0·8)	3·89 (+ 2.2)	3·42 (— 5.8)
18.10	3.97 (+3.3)	2.89 (—4.4)	3.53 (+ 4.9)	4·05 (+ 6·6)	3·35 (—7.6)
27.45	3.95 (+2.9)	2.88 (— 4.8)	3.63 (+ 8.1)	4·20 (+10·4)	3·31 (—8.7)
42.50	4.04 (+5.2)	2.87 (— 5·1)	3.72 (+10·6)	4·56 (+20·0)	3·34 (—7·9)
71.45	4·08 (+6·2)	2·84 (— 5·9)	3·80 (+13·0)	4·83 (+27·1)	3·35 (— 7·6)

These experiments indicate very satisfactorily that the absorption of water by the leg, as a whole, is essentially dependent upon the state of the colloids contained in it. The development of an "œdema" in it is due to the production of acids under these circumstances in the tissues. Just as salts counteract the effect of an acid in favoring the swelling of a (hydrophilic) emulsion colloid, not only according to their concentration but also according to their chemical character, so also do they counteract the œdema of an amputated frog's leg. Non-electrolytes which are ineffective in reducing the amount of swelling of such a colloid in an acid solution are also incapable of reducing the absorption of water by an amputated frog's leg.

3.

We will now pass to the last link in our chain of evidence in favor of the conception of œdema we are trying to establish. This consists in proving that *any condition which makes for the production of acid in the tissues leads to the development of an œdema if a source of water is available.*

The quickest way to put the tissues of an animal into a condition that permits of the development of acids in them is to *kill the animal.* The fact does not surprise us, therefore, that an œdema develops with greater ease in a dead animal than in a living one. If a living frog is kept up to its neck in distilled water it suffers little variation in weight. A change in weight of 3 per cent. covers the extremes. But let the frog be killed and be kept similarly covered with water and a progressive rise in weight at once sets in.

This is readily apparent from the following experiments: Three frogs which had suffered no appreciable change in weight after residence for several days in distilled water, had the urine expressed from their bladders, were killed and weighed (January 3, 1909), and then hung into jars containing distilled water. The original weights of the freshly killed frogs were as follows:

49.5	34.3	39.2

After the designated number of hours in distilled water the weights changed to the following. In parentheses after each weighing is given the percentage of increase in weight (water absorption) as calculated in terms of the original weights of the frogs:

Hours.	%	%	%
10.15	54.8 (+10.7)	39.8 (+16.0)	43.2 (+10.2)
22.00	57.9 (+17.7)	42.2 (+23.0)	45.0 (+14.7)
33.15	59.1 (+19.4)	42.9 (+25.0)	46.8 (+19.3)
52.15	63.0 (+27.2)	46.0 (+34.1)	49.8 (+27.2)
74.00	69.5 (+40.4)	49.2 (+43.4)	55.5 (+41.5)

It is not necessary that the entire body of the frog be covered with water in order to allow such an œdema of the dead to develop. The dead body need only be in contact somewhere with a source of water. In the following experiments only a fraction of the bodies of the dead animals was immersed in water. At 5 P.M., July 19, 1909, five frogs were killed and placed in separate jars, each containing a few cubic centimeters of water. The original weights of the frogs were as follows:

40.0	38.5	35.0	30.5	28.0

Nineteen hours later the frogs had gained in weight thus:

55.5 (+38.7%)	48.6 (+26.2%)	46.0 (+31.4%)	39.5 (+29.4%)	36.5 (+30.3%)

But we possess subtler methods of producing abnormal amounts of acids in the tissues than by killing our frogs. We can use any one of a long series of *poisons*. I chose those which Araki used in his experiments on the effects of lack of oxygen. The introduction of these poisons into the bodies of warm or cold-blooded animals he found to be always followed by the production of excessive amounts of various acids (particularly lactic acid) in the tissues. In a series of experiments made with Gertrude Moore, we found that the *injection of any of the poisons used by Araki into the dorsal lymph sac of a frog is followed by an œdema. Frogs poisoned with morphine, strychnine, cocaine, arsenic, or*

uranyl nitrate all absorb amounts of water which run from 15 *to* 60 *per cent. of the normal weight of the frog.* A frog that has gained even 15 per cent. in weight is decidedly œdematous. The œdema in all these cases begins to develop within a few hours after the poison is injected, and becomes progressively worse for twenty-four to seventy-two hours. The severer the intoxication the greater the œdema. If the amounts of poison injected have not been too large, and the animal is given a chance to eliminate the poison by renewing frequently the water in which the frog is kept, its œdema may be made to disappear entirely, and the animal come out none the worse for its experience at the end of three to six days.

The following experiments may serve to illustrate what has been said:

Morphine Œdema.

A series of frogs which had been kept in distilled water for several days, had the urine expressed from their bladders, were weighed, injected with various amounts of morphine hydrochlorate or morphine sulphate into the dorsal lymph sac and replaced into separate jars containing enough water to cover the legs (100 c.c.). The changes in weight are indicated in the table. The first figure in each of the columns shows the original weight of the frog. Above it is indicated the amount of morphine injected.

Hours.	0.02 gram morph. hydroch.	0.02 gram morph. hydroch.	0.02 gram morph. hydroch.	0.02 gram morph. hydroch.
	grams	grams	grams	grams
0	36.9 (0)	37.8 (0)	35.7 (0)	41.3 (0)
7.00	.....	.....	.....	46.0 (+11.3)
10.15	40.2 (+8.9)	43.1 (+14.0)	43.2 (+21.0)	.....
22.00	39.0 (+5.6)	43.1 (+14.0)	41.0 (+14.9)	.....
26.00	.....	.....	.....	44.5 (+7.7)
33.15	39.0 (+5.6)	41.1 (+ 8.1)	41.0 (+14.9)	.....
47.30	.....	.....	.....	43.5 (+5.2)
52.15	38.8 (+5.0)	39.8 (+ 5.3)	41.0 (+14.9)	.....
74.00	37.0 (+0.3)	37.5 (— 0.8)	38.5 (+ 7.8)	.....
127.00	36.8 (—0.3)	.....	38.0 (+ 6.4)	.....

Hours.	0.04 gram morph. hydroch.	0.08 gram morph. hydroch.	0.05 gram morph. sulph.	0.037 gram morph. sulph.
	%	%	%	%
0	42.7 (0)	62.0 (0)	48.7 (0)	40.2 (0)
3.30	.....	.....	50.7 (+ 4.1)	45.5 (+13.1)
7.00	48.4 (+13.3)	71.9 (+15.9)	.....	.....
18.00	.....	.....	58.0 (+19.0)	53.5 (+33.0)
22.00	.....	.....	59.0 (+21.0)	Dead
26.00	49.0 (+14.8)	76.2 (+22.9)	Dying	
47.30	45.0 (+ 5.4)	70.5 (+13.7)		
90.30	45.0 (+ 5.4)	70.2 (13.2) (Still in strychnine-like spasms)		

Arsenic Œdema.

Three frogs that had been kept in distilled water for four days had the urine expressed from their bladders, were weighed, and injected with the indicated amounts of Fowler's solution. The following table of weights is self-explanatory:

Hours.	0.25 c.c. Fowler's solution.	0.187 c.c. Fowler's solution.	0.125 c.c. Fowler's solution.
	%	%	%
0	45.0 (0)	40.0 (0)	38.9 (0)
6.15	50.0 (+11.1)	47.3 (+18.2)	39.0 (+ 0.2)
18.15	Dead	54.0 (+35.0)	43.0 (+10.5)
24.15	.....	57.0 (+42.5) just died	43.0 (+10.5)

Uranium Œdema.

Six frogs were injected with the indicated amounts of uranyl nitrate and placed in separate glass jars each containing 100 c.c. distilled water. The variations in weight are easily understood from the following table:

Hours.	0.24 gram.	0.24 gram.	0.2 gram.
	%	%	%
0	52.3 (0)	52.1 (0)	51.5 (0)
17.00	58.0 (+10.9)	59.5 (+14.2)	61.8 (+20.0)
22.30	61.0 (+16.6)	62.2 (+19.3)	65.8 (+27.7)
29.30	64.0 (+22.3)	66.5 (+27.6)	70.5 (+36.9)
45.30	66.7 (+27.5)	71.5 (+37.2)	75.2 (+46.0)
53.45	68.0 (+30.0)	75.5 (+44.9)	79.5 (+54.3)
71.00	Killed	77.5 (+48.7)	83.0 (+61.1)
78.00	.....	Dead	Dead

Hours.	0.2 gram.	0.16 gram.	0.16 gram.
	%	%	%
0	51.3 (0)	41.0 (0)	37.8 (0)
17.00	61.2 (+19.3)	52.2 (+26.8)	47.5 (+25.7)
22.30	63.3 (+23.4)	55.8 (+36.1)	48.3 (+27.7)
29.30	64.5 (+25.7)	61.5 (+50.0)	52.0 (+37.6)
45.30	65.0 (+26.7)	65.5 (+59.7)	53.8 (+42.3)
53.45	69.0 (+34.5)	Dead	57.0 (+50.7)
71.00	69.0 (+34.5)	....	58.0 (+53.4)
78.00	71.0 (+38.4)	.....	Dead
	Killed		

In another series of five frogs several injections of uranyl nitrate were made into the dorsal lymph sacs, as indicated below, and with the following results:

Hours.	0.04 gram.	0.04 gram.	0.03 gram.
	%	%	%
0	51.3 (0)	53.2 (0)	46.2 (0)
20.00	55.5 (+ 8.2)	55.3 (+ 3.9)	48.0 (+ 3.9)
	Uranyl nitrate 0.08 gram.	0.08 gram.	0.06 gram.
25.00	56.5 (+10.1)	54.0 (+ 1.5)	47.5 (+ 2.8)
32.30	59.5 (+15.9)	55.0 (+ 3.4)	49.0 (+ 6.0)
	Uranyl nitrate 0.3 gram.	0.24 gram.	0.2 gram.
47.30	61.0 (+18.9)	54.0 (+ 1.5)	50.0 (+ 8.2)
53.00	66.0 (+28.6)	58.5 (+ 9.9)	54.5 (+17.9)
67.00	71.0 (+38.4)	67.0 (+25.9)	63.0 (+36.3)
71.30	Killed	Killed	64.5 (+39.6)
77.00	....	.....	Dead

Hours.	0.03 gram.	0.02 gram.
	%	%
0	45.5 (0)	38.0 (0)
20.00	48.5 (+ 6.6)	41.0 (+ 7.9)
	Uranyl nitrate 0.06 gram.	0.04 gram.
25.00	48.5 (+ 6.6)	39.0 (+ 2.6)
32.30	50.0 (+ 9.9)	40.5 (+ 6.5)
	Uranyl nitrate 0.16 gram.	0.08 gram.
47.30	50.8 (+11.6)	39.5 (+ 3.9)
53.00	53.7 (+18.0)	41.5 (+ 9.2)
67.00	60.0 (+31.8)	45.0 (+18.4)
71.30	61.5 (+35.0)	43.0 (+13.1)
77.00	63.2 (+38.9)	42.2 (+11.0)
88.30	65.8 (+44.6)	41.5 (+ 9.2)
97.00	68.5 (+50.5)	42.0 (+10.5)
115.00	77.5 (+70.3)	45.5 (+19.7)
120.00	Dead	45.5 (+19.7)
126.30	....	45.0 (+18.4)
138.30	.....	48.0 (+26.3)
143.00	.....	49.5 (+30.2)
		2 days later, dead.

These chemical œdemas, as we may call them for short, are of more than academic interest. Inasmuch as we find in the list of poisons enumerated above, heart poisons, kidney poisons, nerve poisons, poisons that increase or decrease blood pressure, that increase or decrease lymph flow, that injure bloodvessel walls, or have not been proved to do so, etc., do we not, first of all, seriously question every theory of œdema that would establish any one or all of these conditions as the primary cause of all œdemas? Secondly, these chemical œdemas have interesting clinical parallels. The œdema of arsenic poisoning and of poisoning by certain other metals is a well-known condition. We are also able to understand how, after the administration of morphine, chloroform, ether, and alcohol (save in small amounts), a certain degree of œdema may develop, or at least a fall in urinary secretion and an increased thirst be noted. All these substances make for a lack of oxygen and an abnormal production of acids in the tissues. At least part of the effects of these various substances may, therefore, be satisfactorily explained *through their effect upon the tissues generally whereby these become œdematous.* Associated with this there must be a fall in urinary secretion (see Section IX, on the Kidney) and thirst. A final question of interest in connection with these chemical œdemas (with which we must class the œdema of kidney disease) is the *distribution of the œdema in clinical cases.* These chemical œdemas are always more general, and, as is well known, are particularly liable to first affect the connective tissues of the face, particularly the eyelids. Other things being equal we would expect in a general intoxication those tissues which are most capable of swelling to be the first to give ocular evidence of the existence of an œdema. It is interesting, therefore, that of the various tissues examined in this regard I found the connective tissues of the orbit not only to be possessed of colloids most sensitive to low concentrations of acid, but also to have weight for weight the greatest affinity ("specific affinity") for water.

VII. ON THE ŒDEMA OF SPECIAL ORGANS.

1. On the Nature and Cause of Glaucoma.

From a pathological standpoint, glaucoma represents simply one of the local œdemas, and from a clinical point of view, all the symptoms and signs of this condition are considered referable to the increased intraocular pressure induced through the abnormally large amount of water held by the eye in this condition. How does the eye come to hold such an increased amount of fluid?

A glance at any of the standard works on ophthalmology[1] shows no dearth of attempts to answer this question, but experiments planned to support the views advanced by the various authors have been singularly unsuccessful. For the most part, when not simply referred to the occult properties of "living" matter, these explanations are identical with those given for œdema anywhere else in the body. They are familiarly mechanical in character in that an increased lymphatic or blood pressure is supposed to *force* an abnormally large amount of liquid into the tissues of the eye. Such increased pressures are generally held to be induced through interference with the outflow of lymph or blood from the eye occasioned through obliteration of the "filtration angle," etc.

The experiments which we have detailed in a previous section of this paper (see Section IV, paragraph 2), and which were instituted in order to ground experimentally the conception of œdema which forms the theme under discussion, showed very clearly that *the most intense grades of glaucoma can be induced experimentally in an eye in the entire absence of any circulation.* This fact coupled with the well-known observation that an increase of the pressure of the circulating liquids through the eye is not followed by glaucoma arraigns all explanations of glaucoma which look to an increased pressure as of essential importance

[1] See, for example, Ernst Fuchs, Augenheilkunde, Dritte Auflage, Leipzig u. Wien, 1893, 393; Priestley Smith, Glaucoma, London, 1891.

in its causation. We are at the same time led to conclude that *the cause of glaucoma may well reside in the tissues of the eye itself*, and that it becomes glaucomatous not because fluid is pressed into it, but because through changes in it, it *absorbs* an increased amount of water. That the amount of such absorption is sufficient to explain the severest grades of glaucoma ever observed clinically, is clearly enough evidenced by the fact that through the mere presence of a little acid, a beef eye can be made to absorb enough water to rupture its enormously thick sclera. This is a grade of glaucoma that exceeds anything that we ever have the opportunity of observing clinically. Our experiments further show that *this increased absorption of water by the eye is dependent upon the colloids in the eye, for not only is the eye built up of a series of different colloids (sclera, cornea, lens, vitreous humor), but the same conditions which govern the absorption of water by fibrin also govern the absorption of water by the eye.* On the ground of these experiments *we can, therefore, no longer insist that an eye becomes glaucomatous because water is forced into it. It does this because chemical changes occur within the eye which increase the affinity of the ocular colloids for water so that these are enabled to absorb water from any available source.* In our experiments with enucleated eyes this source is the solution into which the eye has been dropped; in the body it is the liquids flowing about or through the eye.

Just what are the chemical changes in the eye in clinical cases of glaucoma we are not able to say definitely; but there can be little doubt that the cause of this œdema is in essence the same as that of any of the more generalized ones. In a large number of glaucoma cases, circulatory disturbances in the eye which permit of an accumulation of carbon dioxide and the abnormal development of such acids as are a constant accompaniment of states of lack of oxygen, are unquestionably present. In the glaucomas due to infections or, in general, toxic agents capable of producing inflammatory changes (in the strict pathological sense of the term) in the eye, we have to look to the chemical changes induced by these for the cause of the altered affinity of the ocular colloids

for water.[1] The best evidence in support of this colloidal conception of glaucoma is, however, not furnished by these mere hypothetical discussions, but by the following clinical observations.

2. On the Relief of Clinical Cases of Glaucoma by Subconjunctival Injections of Sodium Citrate.

The experiments which I have described on the swelling of enucleated eyes made us familiar not only with ways and means by which an intense glaucoma can be induced in an eye, but they showed us also how *the development of such a glaucoma can be prevented, or, once established, be made to go down again.* While under ordinary circumstances little is to be gained by simply reducing an œdema, there exist a number of clinical forms which are in themselves dangerous. Glaucoma is one of these, which through its existence for even a short time may permanently blind an eye. To be able to combat the œdema in such a case is, therefore, not a useless procedure.[2]

In the experiments on the swelling of eyes we became familiar with the fact that the presence of any salt markedly decreases the amount that an eye will swell in an acid solution. The question, therefore, arose whether the instillation of salt solutions into the eye might not be followed by relief in clinical cases of glaucoma.

Hayward G. Thomas and I decided to test the matter. The instillation of salt solutions was not, however, to be entered into hastily, for my experiments had shown that *while all salts reduce the amount that an eye will swell in an acid solution, a large number*

[1] Under the influence of proteolytic ferments ordinary gelatine can be converted into Beta-gelatine. As already pointed out, Wolfgang Ostwald's studies show this to be capable of greater swelling than the unchanged gelatine. It is therefore conceivable that in inflammation (whether in the eye or elsewhere) an increased affinity of the tissue colloids for water and a consequent œdema may result merely in consequence of the "autolytic" changes that occur in the injured tissues, even when no abnormal storage or production of acids in the part occurs.

[2] Œdema of the larynx, œdema of the kidney (acute suppression of urine), and œdema of the brain (for example after traumatism) are also dangerous. All these are theoretically reducible through salt solutions of the right kind and concentration. Pulmonary œdema also belongs in this class, but presents a more complex problem than the other ones so far as reduction is concerned.

also increase the tendency to the development of corneal opacities. There would be little gained, except so far as relief from certain of the subjective symptoms might be concerned, by guarding an eye from blindness through glaucoma while blinding it through the agency employed for the relief of the glaucoma. *There exist, however, a number of salts which inhibit markedly the swelling of eyes in acid solution and at the same time not only do not increase but even decrease the tendency to the development of these corneal opacities.* In other words, the use of these salts tends to prevent the development of even that well-known turbidness of the cornea which is so constant a sign in clinical cases of glaucoma, and which one never fails to get in the experiments on eyes that I have described. (See the succeeding paragraph 4 of this section.) These salts are the citrate, tartrate, sulphate, and phosphate of sodium and potassium. After a number of preliminary tests we chose sodium citrate as the salt best adapted for use in clinical cases of glaucoma. We use only the chemically pure salt (Kahlbaum) in concentrations varying from a $\frac{1}{3}$ to a $\frac{1}{6}$ molecular solution. Expressed in percentage, the former is equivalent to a 4.05 per cent. solution, the latter to a 5.41 per cent. solution of the ordinary crystallized sodium citrate ($Na_3C_6H_5O_7 + 11\ H_2O$). The $\frac{1}{3}$ molecular solution has an osmotic pressure below that of the human tissue fluids, the $\frac{1}{6}$ molecular solution one that is slightly above. The injections are made with a fine needled hypodermic under the conjunctiva in the usual manner adopted by ophthalmologists and are preferably preceded by the use of cocaine and adrenalin solutions. Enough of the sodium citrate is injected to gently distend the connective-tissue spaces (5 to 15 drops). Immediately following the injection the patient suffers some pain. While this is usually insignificant, it is fairly severe in certain cases. When this is true, alternate hot and cold compresses laid over the eye ease the pain. In any event it disappears in a few minutes. In the severer cases of glaucoma we use the stronger sodium citrate solution, in the milder cases or for subsequent treatment the $\frac{1}{3}$ molecular solution is sufficient. This will, in fact, rapidly reduce the tension in even the severe cases

of glaucoma. Later in the treatment a mixture of one part of the $\frac{1}{8}$ molecular sodium citrate solution, with two to four parts of a "physiological" (0.9 per cent.) sodium chloride solution, is sufficient.

Up to the present writing we have had opportunity to study and treat ten patients with glaucoma,[1] in all about eighteen eyes. Our results may be summed up as follows:

The use of subconjunctival injections of $\frac{1}{8}$ to $\frac{1}{6}$ molecular (4.05 to 5.41 per cent.) solutions of chemically pure sodium citrate in clinical cases of glaucoma is entirely harmless and is always followed by a prompt fall in ocular tension. The fall in tension is appreciable within ten minutes after the injection, and may be so great as to make the eye have a subnormal tension. The effect of such a subconjunctival injection lasts for from three to six days (or even more) and is accompanied by a relief of all the subjective symptoms of glaucoma (except, of course, the blindness due to structural changes).

It must be clearly understood that when such subconjunctival sodium citrate solutions bring about a diminution in the tension of a glaucomatous eye this does not constitute a "cure" for glaucoma. As a cure of glaucoma we could only consider a removal of that condition or conditions which are responsible for the development of the substances which increase the affinity of the ocular colloids for water. If these are acids, the product of a circulatory disturbance or of an infection, then clearly the real cure for the glaucoma resides in a correction of the circulation to the eye, or in the removal of that infection. But even toward this end the sodium citrate injections can help. In the progressive development of a glaucoma the swelling of the colloids tends to compress the bloodvessels passing into and out of the eyeball. The natural tendency of a glaucoma is, therefore, to make itself worse. Writers on ophthalmology are in the habit of laying great stress on the *obliteration of the filtration angle. This is frequently said to be the cause of glaucoma. It is much more probably a con-*

[1] For a detailed clinical report of half of these see Thomas and Fischer, Annals of Ophthalmology, 1910.

sequence, as evidenced by the fact that enucleated eyes rendered artificially glaucomatous by being placed in acid solutions show the same progressive decrease in the depth of the anterior chamber that is noted in clinical cases. The matter is easily explained through the unequal swelling of the different colloids of the eye, those posterior to the lens (sclera, choroid, vitreous) being capable of greater swelling than those anterior to it (cornea, aqueous).

Through this unevenness in swelling the ciliary body is crowded against the sclera—a process in which the bloodvessels of the ciliary body become pinched. Such an embarrassment in the circulation (lack of oxygen, accumulation of CO_2 and acids) is then added to whatever conditions are already active in producing the glaucoma. To reduce the swelling of the ocular colloids, even though only temporarily, is, therefore, to improve the circulation through the eye and in this way to contribute not inconsiderably toward the restitution of normal conditions within the eye. If the glaucoma is the consequence of some acute condition, then its prompt relief may not only save the eye from blindness through pressure, but by helping toward the reëstablishment of a normal circulation through the eye furnish the necessary conditions required in the repair of all pathological processes.

There is a marked tendency in the recent literature on the treatment of glaucoma to urge more strongly than formerly the use of myotics and constitutional remedies for the relief of glaucoma. This has very largely grown out of the fact that iridectomy all too often fails to give more than temporary relief. The medical means at our disposal have as their main object the mere reduction of tension in the eye. All too often the recognized remedies barely affect the ocular tension, and the relief obtained is unsatisfactory. These sodium citrate injections, therefore, seem to mark a distinct therapeutic advance, for they *always* reduce tension, and promptly. Whatever improvement can be hoped for through simple reduction of the ocular tension can therefore be expected with greater confidence when sodium citrate injections are used than when any of the other customary medical means are employed. But even should a surgical procedure ultimately be deemed

necessary or advisable, the surgical difficulties and dangers arising at times from having to operate upon eyes with a high tension may be entirely controlled through previous subconjunctival sodium citrate injections.

3. Isolated Observations on the Reduction of Clinical and Experimental Forms of Œdema.

I would like to introduce here a series of isolated observations and facts regarding œdema that not only find a ready explanation on the basis of the colloidal conceptions of œdema advanced in this paper, but give them valuable support.

First of all, a series of *observations made on frogs* with intense œdemas following uranyl nitrate injections are of interest. It was to be expected that just as various salts are capable of reducing the swelling (œdema) of fibrin, gelatine, muscles, whole frogs' legs, enucleated eyes, and the tension in clinical cases of glaucoma, they ought similarly to be able to reduce these œdemas of living frogs. As the following shows, they do really do so. A frog that weighed originally 52 grams was injected with 0.24 gram uranyl nitrate and placed in a little distilled water. A progressively increasing œdema set in, so that on the third day after injection the frog weighed 66 grams, a gain of 26.7 per cent. The animal was now placed in a $\frac{1}{4}$ molecular sodium chloride solution. Twelve hours later its weight had dropped to 62 grams. It was now placed in a $\frac{1}{4}$ molecular sodium citrate solution. At the end of another five and one-half hours the œdema had disappeared entirely and the animal weighed only 53 grams. Similarly a frog weighing 51.3 grams was injected with 0.2 gram uranyl nitrate. On the fourth day its weight had risen to 71 grams, a gain of 38.4 per cent. After twelve hours in a $\frac{1}{4}$ molecular sodium citrate solution its weight dropped to 57 grams, which represented an increase of only 11.1 per cent. over its original weight.

John D. Long, of the United States Public Health and Marine Hospital Service, has made entirely similar observations on *clinical*

cases of œdema. His first observations were made on a marine with an œdema of the tissues about the knee due to a tuberculosis of the joint. Finding that his pain was much relieved by bandaging the knee with cloths soaked in sodium citrate solution, Long suggested its injection. With the full consent of the patient, who had been suffering extreme pain for a month past, four small injections were made into the œdematous tissues around the knee well away from the joint. The œdema disappeared promptly in the neighborhood of the injections, and only slowly returned. Equally good results followed a second injection. For several days after each the pain was markedly less, so that when I was invited to see him, the patient was begging for a third series because his œdema and pain were returning. Long has used these injections on other patients with acute and chronic joint affections, and is inclined to attribute much more than theoretical value to them. In this connection it may be noted that the relief of œdema and pain in various acute joint and skin affections experienced when the parts are wrapped in cloths soaked with saturated magnesium sulphate solution, as practised by many physicians, also finds a ready explanation in the action of such amounts of the salt (even though they be relatively small) as are absorbed by the œdematous tissues beneath.

A local disappearance of the œdema can also be obtained in clinical cases when sodium citrate (even in concentrations decidedly below the osmotic concentrations of the tissue fluids) is injected into tissues œdematous in consequence of such conditions as heart disease or nephritis. From a practical standpoint this observation may be of little value; from a theoretical one it is of great interest. Sodium citrate and the other salts that are particularly effective in reducing these clinical and experimental forms of œdema (sodium sulphate, phosphate, tartrate, magnesium sulphate, etc.) constitute the group of the so-called *saline cathartics* and *saline diuretics*. The various experiments on œdema that have just been described bring corroborative evidence for the truth of Franz Hofmeister's[1] belief that the saline cathartics owe

[1] Archiv f. exp. Path. u. Pharm., 1891, xxviii, 210.

their action primarily to an effect upon the colloids of the alimentary tissues—an observation which must seem all the more remarkable because made at a time when our modern enthusiasm over the biological significance of the colloidal state was just being born. But the action of the saline cathartics undoubtedly extends beyond the tissues of the gastro-intestinal tract. Clinically, after a dose of a saline cathartic we are accustomed to find an increased secretion of urine. For this reason we have come to look upon the list of the saline cathartics as identical with the list of the saline diuretics. Undoubtedly the saline diuretics have an action on the colloids of the kidney (see Section IX), but *the various salines also have an action upon the tissues of the organism generally* which has been entirely overlooked. When after a saline purge we notice that the œdema of a patient with heart or kidney disease gets less (or a normal person, for that matter, loses weight) the result is not to be attributed solely to an increased intestinal secretion and diuresis, but in part to an effect upon the colloids of the tissues generally. In consequence of this action upon the tissues generally these give up water to the blood and lymph streams. The blood is then in the same condition as when water is injected into it in a non-thirsting[1] animal, and the excess escapes through the kidney when this is reached. (See Section IX for further details.)

Attention has already been called to the corroborative evidence for our theory of œdema that is furnished by the artificial production of "flea bites" and "urticarial wheals" in gelatine plates. These artificial local œdemas, which mimic so perfectly in shape and rate of development the true bites and stings of insects and the urticarial eruptions in man, can be made to disappear by applying a little ammonia water or calcium chloride to them. May we not find herein an explanation of the beneficent therapeutic effects of local applications of the former and the internal administration of the latter in these very conditions?

[1] Which simply means that the tissue colloids (particularly of the mouth and pharynx) are saturated with water.

4. On the Nature of Corneal Opacities.

In clinical cases of glaucoma there is noted as one of its most constant signs more or less opacity of the cornea. In an entirely similar manner the cornea loses its transparency in the experimentally induced glaucomas that were described above. Inasmuch as the essential change in the eye in glaucoma consists of an abnormal increase in the amount of water held by the eye, the view generally advanced by ophthalmologists that the opacities of the cornea noted in glaucoma are due to the absorption of water by the cornea does not surprise us. Such an origin for the opacities has been extended to include the other transparent media of the eye. Especially has the lens been believed to owe its loss of transparency in many conditions to an imbibition of water.

Serious objections seem never to have been raised against such a view, and this in spite of the fact that clinical cases of absolute opacity of the cornea or the lens may exist without any evidence of an increased absorption of water, while, on the other hand, very severe cases of glaucoma may come and go without more than a mere haziness of the cornea.

The remarks of these paragraphs confine themselves to the question of the origin of *corneal* opacities, simply because these have been studied with greatest care. It seems from preliminary experiments, however, that what is here said regarding the cornea holds also for the lens and the other transparent media of the eye. The opacities in the eye to which these remarks refer necessarily include only such as are the consequence of chemical disturbances in the eye, and have nothing to do with the deposits of leukocytes, formation of connective tissue, etc., which may also give rise to opacities.

Neither the presence of an increased or a decreased amount of fluid in the cornea is responsible for the appearance of an opacity. An opacity is produced whenever some of the colloidal constituents of the cornea are precipitated, and depending upon whether such

a precipitation is only slight or very great these opacities vary from such as are barely visible (steaminess of the cornea) to such as are intensely white (leukoma).

The effect of different solutions on the transparency of the cornea was judged in two ways, first in regard to the *rate* at which they permitted the development of an opacity, and second, in regard to the *intensity* of the opacity. The outer limits of the former vary from a few minutes to several days, for the latter from a turbidness scarcely visible to the naked eye to a whiteness like that of boiled albumin. The conclusion drawn above is based upon the following facts.[1]

(*a*) If an eye is simply allowed to dry, no opacity of the cornea develops. Simple loss of water, therefore, does not lead to the development of an opacity.

(*b*) If an eye is laid in distilled water it gains in weight. In this process of water absorption the cornea takes a prominent part, yet no turbidness of this structure develops until quite late. Simple absorption of water, therefore, does not lead to an opacity.

(*c*) The presence of any acid favors the development of an opacity, but the different acids are very unequally powerful in this regard. Nitric acid induces a corneal opacity more quickly than an equinormal oxalic acid solution, and this more quickly than an equinormal hydrochloric acid. Still less powerful in this regard are sulphuric and acetic acids in the order named. Very clearly, therefore, this order in which acids induce corneal opacities is entirely different from the order in which they make eyes swell.

(*d*) We note a further discrepancy between the amount of water absorbed by an eye and the rate of development, or better, the intensity of a corneal opacity as soon as the effect of adding equimolecular salt solutions of different kinds to any acid solution is compared. While every salt reduces the amount of water absorbed by an eye in an acid solution, some salts favor the development of an opacity while others distinctly inhibit it. The citrate, acetate, and sulphate, for example, inhibit the development of a

[1] See Martin H. Fischer, Pflüger's Archiv, 1909, cxxvii, 46.

corneal opacity, while the sulphocyanate, nitrate, bromide, and chloride favor it.

(*c*) The effect of any salt seems to be made up of the algebraic sum of its constituent ions. When a series of salts having a common base are compared, the order of the acid ions is always found to be the same, and when a series of salts having a common anion are compared, the order of the kations is always seen to be the same. The order in which various anions and kations are effective in producing or inhibiting the formation of corneal opacities is indicated in the following two tables, in each of which the ion most effective in producing an opacity is given first, that most effective in inhibiting it last.

Sulphocyanate, nitrate, bromide, chloride, sulphate, acetate, citrate.

Iron (ferric), copper (cupric), calcium, strontium, barium, magnesium, ammonium, sodium, lithium (?).

The order in which different salts, or, as we had best say, different ions affect the production of these corneal opacities is, therefore, an entirely different one from the order in which these same ions affect the absorption of water by the eye. Not only are such ions (sulphocyanate, nitrate, iron, copper) as are most powerful in leading to the development of corneal opacities found in the same group with such as allow the least absorption of water by the eye, but such as inhibit the formation of corneal opacities most powerfully (acetate, ammonium) are in a class with those which have the least effect on the absorption of water.

This absolute disproportion between the amount of water absorbed and the development of a corneal opacity is well illustrated in Figure 50.

In *a* is shown the thickness of the cornea of an eye which has lain in distilled water for thirty-six hours and is still perfectly clear. In *b* we have an eye that has remained for the same length of time in a $\frac{1}{110}$ normal hydrochloric acid solution. The eye burst six hours after being placed in this solution. The cornea is very thick, but only slightly opaque (ground-glass appearance). *c* was left for thirty-six hours in a similarly concentrated hydro-

chloric acid solution, containing magnesium nitrate in addition [20 c.c. $\frac{1}{10}$ n. HCl + 200 c.c. $\frac{1}{3}$ $Mg(NO_3)_2$]. In spite of the fact that the cornea is not swelled - it is thinner even than normal - it has the intensely white color of boiled albumin. About the same condition of affairs is shown in *d*, which indicates the appearance of an eye thirty-six hours after being placed in a $\frac{1}{110}$ normal hydrochloric acid solution plus ferric chloride (20 c.c. $\frac{1}{10}$ HCl +

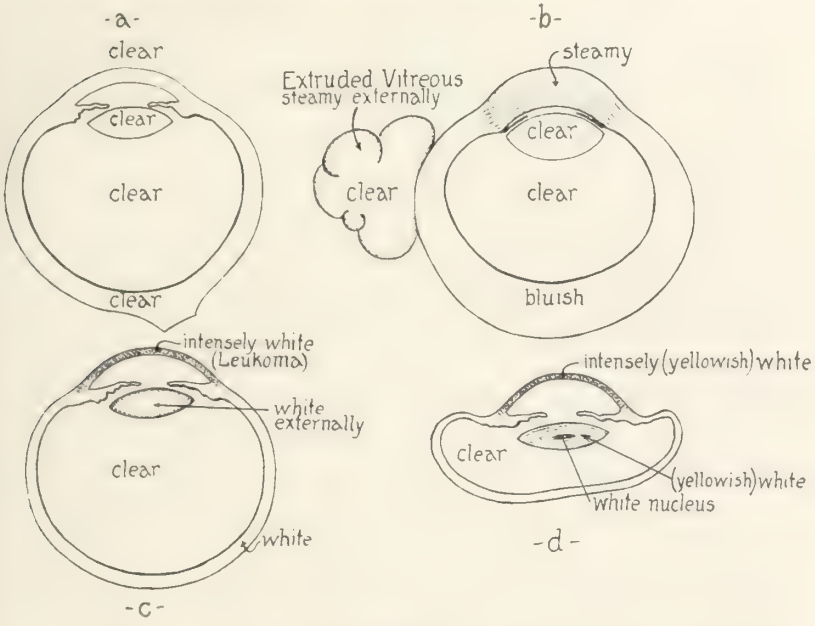


FIGURE 50

200 c.c. $\frac{1}{3}$ m. ferric chloride). In spite of the great loss of water, the thin cornea is intensely white (and stained slightly yellow from the iron chloride).

(*f*) In the experiments on the swelling of eyes it was found that non-electrolytes do not markedly affect the swelling of eyes in an acid solution. Nevertheless, most non-electrolytes appreciably inhibit the development of corneal opacities.

(*g*) All the above facts have shown most clearly how *no* parallelism exists between the amount of water absorbed by the cornea

and the intensity or rapidity of the development of an opacity in it. We need in conclusion only to state that all the facts outlined above are easily harmonized by the conception that a corneal opacity represents the precipitation of a colloid—a protein—within the cornea.

Every statement made above regarding the conditions which favor or inhibit the development of a corneal opacity is merely the parallel of a similar statement familiar to us from the observations of Wolfgang Pauli[1] *on the effects of acids, bases, salts, and various non-electrolytes on the precipitation of protein.*

With this we may conclude our discussion of the essential nature of the opacity of the cornea noted in glaucoma. In the light of our remarks the steaminess of the cornea in clinical cases of glaucoma becomes evidence for the development of acid in the eye in this condition. At the same time, this form of opacity becomes grouped with the opacities that are due to the instillation of silver and copper salts into the conjunctival sac—opacities which we have long been accustomed to regard as protein precipitations (coagulations). We have already pointed out that opacities in the lens and vitreous are undoubtedly of the same character. The chief point to which I would like to call attention in this connection is *the possibility of aiding the absorption of these opacities*, be they in the cornea or in any other of the transparent media of the eye. We generally regard the protein precipitations as irreversible, that is to say, that if once produced they cannot be made to go back into "solution." But this statement is true only in a general sort of a way. The length of time that a precipitate has endured is, first of all, of importance, and second, the exact character of the precipitate. If, for example, it has been produced by a heavy metal it is less reversible than if produced by a lighter one. The important part is that there seems always to exist *some* degree of reversibility.

This fact is of great clinical importance. It accounts, first

[1] Hofmeister's Beiträge, 1903, iii, 225; 1904, v, 27; 1906, vii, 531. Note particularly the effect of different salts on the precipitation of protein which carries a positive charge due to the presence of free hydrogen ions.

of all, for the disappearance of the steaminess of the cornea in attacks of glaucoma. But more than this, the very important fact suggests itself, that through the use of proper salt solutions we ought not only to be able to inhibit the development of opacities in the transparent media of the eye, but also aid their absorption ("solution") after once having been formed. It was found above that the presence of citrate (sodium citrate) not only does not favor, but actually inhibits the formation of opacities. It was this fact, together with its great power of reducing the affinity of colloids for water, that made this salt the one of choice for subconjunctival injections in glaucoma. But the question naturally suggested itself whether the same salt injections might not favor the solution of opacities even in cases not associated with an increased tension. Hayward G. Thomas is testing out this matter in a series of eyes with diminished vision due to opacities in the cornea, lens, and vitreous. He has noted a decided improvement in all studied thus far, and has obtained this to a degree and at a rate that cannot be attributed to the mere "spontaneous" improvement frequently noted in these cataractous and other eyes.

5. On the Passive Congestion Œdemas of the Kidney and the Liver.

We have had placed at our disposal through the discussion of œdema in these pages a series of facts which are of interest in the special problem of the so-called passive congestion œdemas of the kidneys and the liver. In consequence of the interference with the outflow of blood from these organs, be this due to a merely local disturbance, such as pressure upon the efferent vein, or to a more general one, such as heart disease, they become overfilled with blood and a general increase in the size of the organs is noted. This increase in the size of the organs is entirely independent of the accidental presence of an excessive amount of blood in the organ; it is due, in other words, to an increase in the size of the individual cells and tissues—an œdema. For this œdema of the parenchymatous organs the same factors of

increased blood pressure, increased permeability of bloodvessel walls, etc., that are so familiar to us from our previous considerations, have again been held responsible in fact, the deductions that have been made from a consideration of the well-defined passive congestion œdemas of various organs as observed clinically or produced experimentally may be said to have colored our conceptions of the essential nature of all other classes of œdema.

There exists no dearth of isolated experimental and clinical observations on the passive congestion œdemas of the liver and the kidney, but the various attempts that have been made to correlate these facts into a satisfactory theory can hardly be said to be successful. The adherents of the pressure theory, for example, cannot meet the gross fact that evidence of any increase in blood pressure is all too often absent in clinical cases of marked "congestion" of the kidneys or liver, that the enlarged passively congested organs decrease in size after the use of drugs whose chief action makes for an *increase* in blood pressure, and that enormous experimental increases in blood pressure in animals do not lead to œdemas of these organs. Believers in the increased permeability of bloodvessel walls have never proved their point physicochemically, nor have those who have recently resurrected the role of hydræmia forty years after Cohnheim buried it *experimentally*.

In the light of our colloidal conceptions of water absorption, how must we interpret the phenomena that characterize the passive congestion œdemas of the kidneys and the liver? *The cause of the œdema is again to be sought in the tissues. The circulatory disturbances leading to an œdema of these organs all have this in common: they lead to a state of lack of oxygen in the tissues in consequence of which acids are produced in them. These acids increase the affinity of the tissue colloids for water, whereby they are enabled to absorb an increased amount of water from any available source.* This idea is supported by the following:

(*a*) It is a well-known fact that when the efferent (renal) vein of the kidney is tied in animals, the organ becomes filled with blood, and that the kidney tissues proper swell and become progressively firmer in consistence. This is the typical picture of

A *B*

FIGURE 51.—*A*, normal right kidney; *B*, œdematous left kidney of the same rabbit twenty-three hours after ligation of the renal artery. Experiment "IV" of May 13, 1909.

a passive congestion sufficiently severe to permit of the development of an œdema in the congested area. We need not repeat that what happens in this experiment is usually interpreted as an œdema due to an increased blood pressure, alterations in vascular permeability, etc. All these explanations fall as soon as it is stated that *ligature of the renal artery leads to the same series of changes in the kidney as ligature of the renal vein* (with the exception of the overfilling of the bloodvessels). (See Figure 51.)

An abstract of a few experiments carried out with Gertrude Moore on rabbits may serve to illustrate this point. In a series of nine Belgian hares we ligated the left renal vein in three and the left renal artery in the remaining six. The operations were made under morphine anæsthesia, and in no case consumed more than five minutes. None of the operations were complicated by infection. At various periods after the operations the animals were killed and the two kidneys of each animal weighed. As is clearly apparent from the following tables, the increase in the weight of the kidney after ligature of the artery is quite as great as after ligature of the vein. The extra amount of clotted blood found in the kidney when the veins are ligated easily accounts for the somewhat higher values found in Table W over those found in Table X.

TABLE W.—*Ligation of Left Renal Vein.*

Rabbit.	Weight of rabbit.	Hours after ligation.	Weight of kidneys. Normal.	Ligated.	Gain in weight in % of normal.
May 13-09 "VI"	930	19.20	4.20	7.00	66.6%
May 1-09 "C"	1500	22.10	7.50	12.70	69.3%
May 13-09 "V"	811	42.40	3.80	13.95[1]	267.1%[1]

[1] This unusually high figure was due to the fact that an enormous extravasation of blood into the capsule with œdematous swelling occurred in this case.

TABLE X.—*Ligation of Left Renal Artery.*

Rabbit.	Weight of rabbit.	Hours after ligation.	Weight of kidneys. Normal.	Ligated.	Gain in weight in % of normal.
May 13-09 "I"	970	4.25	5.60	6.50	16.1%
May 13-09 "III"	1127	19.00	5.07	7.95	56.8%
May 13-09 "IV"	1115	23.00	4.75	7.42	56.4%
May 1-09 "A"	1500	23.00	7.43	11.70	57.3%
May 13-09 "II"	734	42.15	3.63	6.65[1]	83.2%[1]
May 1-09 "B"	1560	48.00	7.40	10.65	43.9%

[1] This high value was due in part to an extravasation of blood into the capsule with œdematous swelling. Note that the escape of blood occurred after ligature of the artery (diapedesis without blood pressure)!

A decrease in blood pressure is, therefore, quite as effective in bringing about an œdema of the kidney as an increase. While such a result is unexplainable on the basis of the widely accepted pressure theory of œdema it is not surprising to us. In fact, such an experimental result was anticipated. Ligation of the vessel which carries the arterial blood to an organ must of necessity lead to a state of lack of oxygen in the tissues quite as readily as ligation of the vessel which carries the venous blood away.

We may turn now to a consideration of the *liver*, where, owing to the anatomical peculiarities of its vascular supply, valuable conditions are offered for experiments with which to further test this colloidal conception of œdema.

The kidney is supplied with blood through the renal artery, which it will be recalled is very large as compared with the size of the organ. The physiological purpose of this anatomical arrangement is not far to seek. Through this artery there must pass to the kidney not only enough blood to supply the kidney tissues with oxygen, but all that blood from which the kidney separates the urine. In the case of the liver the blood supply is quite different. Through the venous *portal blood* the characteristic functions of the liver are subserved; through the arterial blood furnished by the *hepatic artery* the parenchyma is supplied with its necessary oxygen. Both these streams unite to leave the liver through the *hepatic vein.*

When now we see a liver become decidedly œdematous through passive congestion, say in consequence of a heart lesion or pressure upon the hepatic vein, how is this result to be interpreted?

After our remarks on the essential role played by lack of oxygen, and not mere blood pressure changes in the œdema of the kidney, it does not surprise us to recall the well-known fact that ligation of the *portal vein* is followed by no grossly apparent morphological changes in the *liver*—the portal vein carries only venous blood to the liver, and so changes in the parenchyma due to the production of acids and a consequent œdema of the hepatic tissues is not to be expected. Quite a different picture is obtained when the *hepatic artery* is ligated. *In spite of the fall in blood pressure*

brought about by this means the liver rapidly develops an intense œdema. This result is quite expected on the basis of our theory, and indicates very clearly that *the real reason why a passive congestion leads to an œdema of the liver is because it interferes with the necessary flow of arterial blood through the organ via the hepatic artery.*

The following four experiments show how quickly a ligation of the hepatic artery in rabbits leads to an œdema of the liver, and how severe this is. The œdema follows ligature the more rapidly and is the more intense the more perfect the ligation of the various branches that constitute the hepatic artery in this animal. The operations were again made under morphine anæsthesia, in ten to fifteen minutes and without infection. The increase in the size of the liver while readily apparent to the eye can be expressed numerically only by indirect calculation of the weight of the liver in percentage of the body weight of the operated animal. In a series of six *normal* rabbits we found the liver to constitute 2.9 per cent., 3.2 per cent., 3.5 per cent., 3.7 per cent., 3.7 per cent., and 3.7 per cent. of the total body weight. The following Table Y shows how much the liver is increased in size when the hepatic artery is ligated.

TABLE Y.

Rabbit.	Weight of rabbit.	Hours after ligation.	Weight of liver at autopsy.	Per cent. of body weight.	Remarks.
May 14-09 "VIII"	845	13	48.5	5.7	One well-defined artery to the liver.
May 1-09 "XX"	694	16	37.3	5.3	One well-defined artery to the liver.
May 14-09 "IX"	867	18	35.7	4.1	Artery has several branches, one only ligated.
May 10-09 "Red"	764	23	33.2	4.3	Several small branches ligated.

b) Having shown by these simple means that the kidneys and liver become œdematous in consequence of various circulatory disturbances only because these disturbances lead to a state of lack of oxygen in the tissues, we have now to say what are the consequences of such a state of affairs. We are especially in-

terested in evidence that shows that under such circumstances an abnormal storage or production of acids occurs in these tissues. The accumulation of carbon dioxide in the cells and tissues is a necessary consequence of any interference with the outflow of blood from (or inflow to) a part. The abnormal accumulation and production of other acids in both kidneys and liver in consequence of a disturbance in oxygen supply to these viscera has, however, been proved directly for these organs by the already oft-quoted experiments of Trasaburo Araki[1] and Hermann Zillessen.[2] Ligation of the renal artery or vein, or ligation of the hepatic artery, is always followed by the production of lactic and other acids in the kidneys and the liver. In these acids, the (hydrophilic) emulsion colloids of the tissues, and an available source of water, we have, therefore, all the conditions necessary for the development of an œdema. When the renal vein is tied the available source of water is found in the blood that attempts to enter the kidney through the renal artery and stagnates in the kidney; when the artery is tied the increased affinity of the tissue colloids for water is satisfied by absorbing it from the blood that backs into the kidneys through the veins. In the clinical cases of passive congestion of the kidneys a ready source of water is, of course, found in such a circulation as continues to be maintained through these organs. When the hepatic artery is tied, or in clinical cases of passive congestion of the liver, a plentiful source of water is found in the portal circulation and the blood from the hepatic vein. On the basis of these colloidal conceptions of water absorption we have also now no difficulty in understanding the well-known physiological fact that an accumulation of carbon dioxide in the arterial blood supply to the kidney, or any interference with the normal oxygen-carrying power of the blood unaccompanied by any changes in blood pressure, leads to an increase in the size of the kidney, in other words, an "œdema"; while an abundant oxygen supply brings about the reverse result. We can

[1] Zeitschr. f. physiol. chem., 1891, xv, 335 and 546; ibid., 1894, xix, 422. See also Hoppe-Seyler, ibid., 1894, xix, 476.

[2] Zeitschr. f. physiol. chem., 1891, xv, 387.

also understand the enlargement of the kidney that is a constant accompaniment of the various acute forms of nephritis. The various toxic agencies which we recognize clinically or experimentally as capable of inducing this pathological state—various toxins, snake venoms, cantharidins, uranium and chromium salts—all belong either directly into the group of the reducing bodies or can be shown experimentally to interfere with the normal oxidations of living cells. But to interfere with these oxidations is followed by the same consequences as ligation of an artery or a vein, so that a swelling of the kidney cells is a logical result. The enlargement of the liver and the kidneys in phosphorus poisoning can be explained on the same ground. As is now well known, the increase in the size of the liver in phosphorus poisoning is not due primarily to an excessive deposition of fat, but to a mere increased amount of water held by the poisoned organ.

(c) The colloidal theory seems, therefore, to harmonize in a very satisfactory way observations which on the basis of other theories seemed contradictory, while it correlates at the same time a series of apparently unattached clinical and experimental facts. Much interest attaches itself in this connection to a series of observations by H. J. Hamburger[1] on the kidney and the liver, and by Waichi Hirokawa[2] on the kidney.

In his studies of the "osmotic" behavior of the kidney, Hamburger found all the diameters of the isolated kidney to increase when he perfused it with blood serum to which an acid had been added, and to decrease when he replaced the acid with an alkali. Isolated kidney cells behave in a way entirely similar to the whole kidney. They swell in water and in weak salt solutions. In sufficiently strong solutions of neutral salts they keep their normal size or even shrink. In these experiments the action of acids and alkalies is entirely unintelligible on the osmotic basis of water absorption, and close scrutiny reveals unexpected disparities between observed and calculated effects of the different salt solu-

[1] Osmotischer Druck und Ionenlehre, Wiesbaden, 1904, iii, 52, and ibid., 50 and 54.
[2] Hofmeister's Beiträge z. chem. Physiologie, 1908, xi, 458.

tions. Our colloidal theory fares better. The perfusion with acidified serum leads to an increased affinity of the tissue colloids for water. When the serum is alkalinized this neutralizes the acid present in the kidney and through the simultaneous reduction in acidity and the production of salt in the tissues the affinity of their colloids for water is decreased, hence shrinkage of the organ. The isolated kidney cells are in a state of lack of oxygen, and become acid after removal from the body. For this reason they swell when placed in distilled water. Salt solutions counteract this swelling, and this the more the higher the concentration of the salt, as experiment proves. The whole series of phenomena is identical with that which was previously described in our experiments on the swelling of fibrin.

Hirokawa also studied the "osmotic" behavior of kidney cells. He found blocks of kidney tissue to be progressively the more capable of absorbing water from increasingly stronger solutions of sodium chloride the longer the blocks of tissue had been out of the animal. Hirokawa correctly attributes this finding to the postmortem production of acid in the tissues, which he believes to increase the affinity of these tissues for water in the same way that K. Spiro found the affinity of gelatine plates raised for water through the addition of a little acid.

Kidney cells, therefore, can become "œdematous" when entirely removed from the body; in other words, when entirely away from any vestige of a circulatory system. It only remains for us to connect the behavior of these "dead" kidneys with that of the passively congested "living" ones in an animal. This is done as soon as we recall the fact that the postmortem production of acids in the tissues, and that which occurs in the absence of an adequate oxygen supply represent identical processes.

Experimental data are at hand which show that in the entire absence of any circulation, liver cells may also show all the signs of an œdema that we are accustomed to look for in an autopsy. H. J. Hamburger[1] found isolated liver cells and blocks of liver tissue to swell in water and in dilute salt solutions, and to main-

[1] Osmotischer Druck und Ionenlehre, Wiesbaden, 1904, iii, 50 and 54.

tain their volume or even shrink if stronger salt solutions or dilute alkalies were added. Dilute acids, including carbon dioxide, markedly increased the swelling. These remarks again parallel the effects of acids, alkalies and salts on the swelling of fibrin in a faintly acid solution.

6. On the Nature and the Cause of Pulmonary Œdema.

The state in which we today find the problem of pulmonary œdema is essentially the same as that in which we find the problem of œdema in general. Much weight is still laid upon William H. Welch's[1] belief that pulmonary œdema is due to "a disproportion between the working power of the left ventricle and of the right ventricle of such character that, the resistance remaining the same, the left heart is unable to expel in a unit of time the same quantity of blood as the right heart." It is readily seen that this theory is a mechanical one which assumes that through a heightened pressure of blood within the pulmonary circulation fluid is squeezed into the tissues of the lung and out into the alveoli and bronchi. According to this conception pulmonary œdema is placed in the general group of Julius Cohnheim's[2] congestion œdemas.

Welch's ideas have not gone unchallenged. Through the observations of various authors, particularly H. Sahli[3] and M. Löwit,[4] it has been proved beyond doubt that the severest grades of pulmonary œdema may exist clinically and be produced experimentally without any evidence of an increased pressure in the pulmonary circuit. Welch's theory has in consequence been variously modified or cast aside entirely. We hear again of "increased permeability of bloodvessel walls," of "hydræmia," of "secretory" disturbances, of still more vague "irritations," and, when all these fail, of changes in the peculiar "life" of the

[1] Virchow's Archiv, 1878, lxxii, 375. The quotation is transcribed from a letter to S. J. Meltzer, American Medicine, 1904, viii, 195.
[2] Allgemeine Pathologie, Zweite Auflage, Berlin, 1882, i, 501.
[3] Arch. f. exp. Path. u. Pharm., 1885, xix, 431.
[4] Ziegler's Beiträge, 1893, xiv, 401.

cells themselves. The views held by the various authors are so divergent and at times so flatly contradictory that a detailed discussion of them is purposeless. The vagueness of these theories stands in sharp contrast to the really excellent experimental and clinical observations that are available. A unifying interpretation of these is clearly still lacking. Toward such the following is offered:

The problem of pulmonary œdema is identical with the problem of the œdema of such an organ as the liver. The reason for this is at once apparent when we call to mind the fact that the vascular arrangement in the lungs is very similar to that which we previously discussed for the liver. Just as the liver, so is the lung supplied with two blood streams—with a venous stream through the pulmonary artery, which only passes through the lung for purposes of oxygenation, and an arterial stream through branches from the thoracic aorta, the bronchial arteries, which supplies the parenchyma of the lung with oxygen. The blood brought through these nutrient arteries leaves the lung in part through the bronchial veins, in part admixed with the blood of the lesser circulation through the pulmonary veins. *The various facts at hand on the experimental production of pulmonary œdema are all easily interpreted as soon as we say that an œdema results whenever the oxygen supply to the parenchyma of the lung is sufficiently interfered with.*

If the pulmonary artery passing to one lung is ligated, no œdema results. If, in addition to this, most of the branches passing to the opposite lung are similarly treated, we still get no œdema. Enough circulation needs only to be maintained through the lung to keep the animal alive. This result is entirely to be expected, for such ligations do not interfere with the oxygen supply to the parenchyma of the lung. Ligation of the pulmonary veins may lead to œdema of the lungs, but only if sufficiently extensive to shut off most of the blood as it returns from the lung. In other words, it is not an easy matter to dam back the blood in the bronchial arteries (which discharge in part into the bronchial veins, in other part into the pulmonary veins) by ligating only the

pulmonary veins. These experiments show that interferences with the pulmonary circulation itself are on the whole scarcely able to lead to an œdema of the lung. The most effective way to bring about a pulmonary œdema is to disturb the *systemic circulation*. Compression of the left ventricle leads to pulmonary œdema, as does also ligation of the aorta either at its root or not lower than the left subclavian artery. Ligation of the thoracic aorta low down, or of the abdominal aorta, does not lead to pulmonary œdema. These undisputed experimental facts are hard to understand on the basis of any pressure theory. While a rise of blood pressure in the pulmonary circuit may well be present in all these experiments, why should it be *more* effective when induced through ligation of the aorta than through direct ligation of the pulmonary vein? And why should ligation of the aorta to just below the left subclavian artery lead to a pulmonary œdema, and ligation just a little lower down be ineffective? Only a few small arteries are given off by the thoracic portion of the descending aorta. We experience no difficulty in interpreting all these findings when we recall that the bronchial arteries leave the aorta just below the left subclavian. Compression of the left ventricle and ligation of the aorta to just below the subclavian all spell a lack of oxygen for the lung parenchyma, and hence an œdema. A ligation just below the bronchial arteries is without effect in this regard.

These experiments show that a pulmonary œdema develops under the same conditions that lead to an œdema in any other organ, namely, whenever its parenchyma is placed in a state of lack of oxygen. This state of lack of oxygen we always discovered to be important in other organs because it led to an abnormal accumulation or production of acids in the tissues. That such conditions prevail when the lungs become œdematous is borne out not only by the fact that a pulmonary œdema is never induced in any animal by the various ligations described above without gross evidences of improper aëration of the blood, but by the following facts regarding chemically induced œdemas, and the œdemas of excised lungs.

Pokrowsky, Friedländer, and Herter[1] found that rabbits and dogs which had breathed for some time an atmosphere rich in carbon dioxide showed grades of pulmonary œdema at autopsy which varied from such as were scarcely recognizable to such as were sufficiently intense to kill the animals. Œdemas have also been noted after inhalation of the fumes of various other acids. Other chemical methods of inducing a pulmonary œdema lead to a state of lack of oxygen and acid production in the tissues in a more indirect way. Under this heading come hydrocyanic acid, various ethers and anæsthetics, carbon monoxide, adrenalin, and iodine—all of them substances which we know interfere markedly with the normal oxidations of living cells.

The clinical evidence that pulmonary œdema is more often an accompaniment of the œdema of nephritis than of the œdema of heart disease is also easily understood on the basis of this chemical origin of pulmonary œdema. In nephritis we have the toxic bodies which the kidneys have failed to excrete and which are responsible for the œdema of the body tissues generally, more or less uniformly distributed throughout the liquid constituents of the various tissues and the blood. The parenchyma of the lungs is therefore as likely to be affected by these toxic bodies as the parenchyma of any other organ of the body. In heart disease, on the other hand, the severity of the œdema of any other organ is distinctly dependent upon the circulation itself in that this determines the amount of oxygen furnished the organ and the readiness with which the carbon dioxide formed in it is carried away. Generally speaking, the greater the distance of an organ from the left ventricle, the poorer must, therefore, be its oxygen supply, and in consequence the greater its opportunity to develop an œdema. In heart disease the lung is, therefore, of all the organs, in the best position to be supplied even to the last not only with the best oxygenated blood available, but with that lowest in carbon dioxide. All this explains why, in spite of much embarrassment in the pulmonary circulation,

[1] Cited from Cohnheim, Allgemeine Pathologie, Zweite Aufl., Berlin, 1882, i, 502, and ii, 273.

an œdema of the lung need not develop. This does not occur until the parenchyma of the lung itself suffers from lack of oxygen. Such a condition need not set in until the systemic blood as it leaves the heart is poor in oxygen and so supplies the lungs with an inadequately oxygenated blood through the bronchial arteries. Hence the so common *terminal* pulmonary œdema. Cohnheim has well said that "man does not die because he develops a pulmonary œdema, but he develops a pulmonary œdema because he is dying." The gradually developing lack of oxygen and the accumulation of carbon dioxide in the lungs in consequence of a gradually failing circulation and respiration account for it without difficulty.

This conception of œdema can be tested in yet another way. If the lung becomes œdematous through any condition which interferes with a normal oxygen supply to the parenchyma, then it ought to be particularly easy to produce an œdema in a lung that has been removed from the body. As a matter of fact, *the most intense ædemas of the lung which simulate in every way those observed at the autopsy table may be produced in lungs removed from the body, and in the entire absence of any such blood pressures as are considered active in the current theories of pulmonary ædema.*

The entire uninjured lungs of sheep freshly obtained from a nearby slaughter house, and with the heart left intact, served for material in these experiments. As injection fluids, I have thus far used water, various salt solutions, dilute acid solutions, and these mixed with salts. As the experiments are not yet complete, I will simply describe the effects of injecting water or a $\frac{1}{6}$ molecular sodium chloride solution into the pulmonary arteries. With the use of either of these fluids an intense pulmonary œdema results. The experiments are carried out in the following way: A cannula is first tied into the pulmonary artery; a ligature is next thrown about the heart below the cannula, and the heart cut off below this ligature. After adherent tags of tissue are removed, the lung is weighed, then hung up by a ligature drawn through the trachea. If, now, a $\frac{1}{6}$ molecular sodium chloride solution or distilled water is simply allowed to *trickle* into a funnel

connected with the glass cannula inserted into the pulmonary artery, the lung takes up enormous amounts of the fluid in a very short time. A lung weighing approximately 500 grams will take up two to three liters of either of these solutions in an hour or two. What becomes of this fluid is very interesting. The lung tissue itself is first affected. It swells up enormously (more than doubling in weight after infusion for an hour or two), and in the earlier periods of the experiment, if the influx of fluid into the pulmonary artery is stopped, the lung may be turned upside down and not a drop of fluid will flow out of either the bloodvessels or the trachea. If the fluid is allowed to continue to trickle into the funnel connected with the pulmonary artery, the pleural surface is, after a time, found to become moist, and soon a drop of fluid falls from the lower edge of the lung. This is soon followed by another and another until a steady drip is established which may allow several hundred cubic centimeters of this "pleural exudate" to collect in the course of an hour in a vessel placed below the lung. At the same time the lung can no longer be turned upside down without obtaining a bloody, frothy fluid from the trachea. This fluid gradually rises in the trachea, and if not removed, overflows. The overflow continues as long as the infusion of water or salt solution into the pulmonary artery is kept up (several hours). Let it be noted that all this time not a drop of fluid exudes out of the veins even though these have not been ligated. *If the infusion is properly regulated the tissues take up all the fluid that passes into the artery, absorb much of it themselves, and "secrete" the rest into the alveoli and bronchi and through the pleura.* Even after the infusion of liquid has been kept up for several hours, only a few cubic centimeters can be recovered from the bloodvessels. From the experiments that have been carried out thus far it can be said that the longer the lungs have been out of the animal, the more quickly do these signs of a pulmonary œdema develop. Of the various injection fluids used, water leads to the greatest œdema of the parenchyma of the lung itself. When any salt solution is used this is not so great, but the evidence of fluid in the bronchi is obtained much

earlier, and this "secretion" is more intense. Sodium citrate and sodium sulphate are more powerful in this regard than sodium chloride. In other words, the saline cathartics and diuretics increase a secretion of fluid into the alveoli just as they increase the secretions from the intestines and the kidneys respectively. (See Section IX, on the Kidney.)

We have thus far spoken of pulmonary œdema as a pathological entity in the sense in which this term is ordinarily used in pathology. But for purposes of discussion and for the ultimate solution of the problem I believe that *we will have to distinguish between the mere presence of an increased amount of fluid in the tissues of the lung proper, and the presence of fluid in the alveoli.* While in the ordinary pulmonary œdema evidence of both is found, greatest weight is usually laid on the presence of fluid in the alveoli and bronchi. When this is found it undoubtedly represents the extreme of what we are pleased to call a pulmonary œdema. Very severe œdemas of the lung may exist without any fluid in the alveoli (as in the earlier periods of the pulmonary œdema of excised lungs). The presence of an excessive amount of fluid in the lung tissues proper and the presence of abnormal amounts of fluid in the alveoli are rather to be regarded as associated, though not identical processes. *We have no difficulty in interpreting all the phenomena of the œdema of the lung tissue itself on the basis of our colloidal theory of water absorption.* The tissues of the lung in pulmonary œdema come to hold an increased amount of water because acids are produced in them. Whether the possibilities for such an abnormal accumulation of acid are offered the lung by ligating various bloodvessels in the body or by taking it out of the body and injecting it with water or a dilute acid is immaterial. That this water absorption is really a colloidal affair is again proved by the fact that all salt solutions inhibit the development of the œdema of the lung tissues proper, not only according to the concentration of the salt employed, but according to the character of the salt. The citrate and sulphate of sodium, for example, inhibit the absorption of water by the lung tissues themselves *more* than the chloride. Yet just the reverse holds

regarding the "secretion" of fluid into the bronchi. It is for this reason that I believe the two processes will have to be dealt with separately. In just what this "secretion" exists *physico-chemically* cannot as yet be said definitely, but that it, too, represents a colloidal problem is clearly enough evidenced by this. All that separates the lumen of the lung capillaries from the alveoli is a colloidal membrane composed of a double layer of flat cells joined together by a little colloidal intercellular substance. The solution of the problem is, therefore, intimately associated with the solution of the physico-chemical problem of how any liquid passes through any membrane. As in this, microcapillary forces, with the important influence of the surface tensions of the liquids that are brought in contact with the membrane, are of first importance, we may well expect to find these of use in unravelling the, at present, mysterious biological phenomena that are encountered in discussing not only this secretion of fluid into the alveoli of the lung (or into the peritoneal cavity, the pericardium or the pleura), but any phase of the general problem of "secretion."

VIII. TURGOR, PLASMOLYSIS, AND PLASMOPTYSIS.

In the earlier pages of this paper, when we were first placing our clinically interesting problem of œdema, we not only described experiments which make this a problem of the cells, but we pointed out that the phenomena characteristic of œdema really represent only the extremes of a series of a phenomena that are exhibited by all cells, vegetable as well as animal. To a brief consideration of this series of phenomena which are found grouped under the general heading of *turgor, plasmolysis,* and *plasmoptysis* we will now turn.

By turgor the plant physiologists understand the normal rigidity of the plant cell as determined by a normal or physiological water content. When by any means the protoplasm of the cell is made to shrink away from the morphological (cellulose) cell wall, the cell is said to be plasmolysed. When, on the other hand, the

protoplasm is made to swell so that the cell wall is ruptured, plasmoptysis is said to have resulted. The animal physiologists have not used these terms in such a strict sense. In the use of the term turgor they agree with the plant physiologists. The term plasmoptysis they do not generally employ at all, and under the heading of plasmolysis they not only consider all the more marked variations in the size of cells both in the way of a decrease or an increase, but also certain phenomena which have become associated with such variations in size, as, for example, loss of coloring matter by the red blood corpuscles (hemolysis). These distinctions in terms must be borne in mind if confusion is to be avoided. To prevent ambiguity in the following paragraphs we will in each case first define our terms.

The reason why the phenomena of turgor, plasmolysis, and plasmoptysis are brought up in this paper is because discussion of their essential nature has not as yet been brought to a satisfactory conclusion. For this reason the following paragraphs which bring a unifying explanation for many of the apparently disconnected and contradictory experimental facts bearing on the problem are not out of order. Again will we find ample evidence of the important role played by the colloids in these general phenomena of water absorption, and thus see an application made to problems considered essentially physiological of certain principles first worked out in the discussion of a pathological state.

1. The Absorption of Water by Spermatozoa, Epithelial Cells, and White Blood Corpuscles.

In the attempt to establish the validity of the laws of osmotic pressure for certain physiological and pathological manifestation of water absorption, biologists have been particularly eager to work with material which on experiment was found to approximate most closely the behavior demanded by theory. It is for this reason that certain plant cells and the red blood corpuscles have

been the subject of more exhaustive study so far as their behavior toward water absorption is concerned than any other cells. The reason why just these cells should have approximated obedience to the laws of osmotic pressure more perfectly than most others that have been studied may appear later. But even these chosen cells show such great exceptions to the behavior demanded by theory that it is impossible to escape the experimentally well-grounded conclusion that *most, if not all, cells do not follow the laws of osmotic pressure.* The attempts that have been made to harmonize the observed behavior of various cells with that demanded on the theory that cells represent osmotic systems are ingenious, but we can scarcely believe sufficiently supported by experiment to be convincing. For the most part the explanations given are complicated, which constitutes in itself a threatening feature when the explanation of any natural phenomenon is hazarded. What strikes one as particularly encouraging about the colloidal idea of water absorption is its simplicity, and the breadth of water absorption phenomena to which it may be applied without apparent experimental or theoretical objection.

In a preceding part of this paper we tried to show how the absorption of water by *kidney* and *liver* cells is essentially a function of their colloidal state. *What was said regarding these cells is also true regarding the behavior of spermatozoa, of white blood corpuscles and of the epithelial cells of the bronchi, intestine, bladder, and œsophagus.* We need not enter into the detailed experimental findings which may be found in H. J. Hamburger's[1] excellent work. Again, we encounter no difficulty in explaining the experimentally observed facts when we call to mind the effect of acids, alkalies, salts, and these in mixture upon the swelling of such an (hydrophilic) emulsion colloid as fibrin. All the cells mentioned swell if placed in distilled water. This fact, which is always interpreted as due to differences in osmotic pressure, is really to be explained by remembering that under the conditions prevailing in these experiments the cells produce acids which

[1] Osmotischer Druck und Ionenlehre, Wiesbaden, 1904, iii, 2 to 33; ibid., 52; ii, 400 to 432.

increase the affinity of their colloids for water. A second factor is found in the diffusion of at least some salts *out* of the cell, for the higher the concentration of the neutral salts in a colloid the less does it swell. The effect of acids, including carbon dioxide, is readily understood. Acids always bring about the greatest amount of swelling in colloids, and they are found to do this also in this biological material. The effects of alkalies is variable. Sufficiently dilute alkalies inhibit the swelling of spermatozoa in water (through the combined effect of neutralization of the acid formed in the spermatozoa and the production of salts) and of epithelial cells and white blood corpuscles suspended in water, salt solution, sugar solution, or serum. In every case the alkali neutralizes the progressive production of acid in these cells, as this occurs under the conditions of the experiments (for example, separation from an adequate oxygen supply, as when the epithelial cells are scraped off a mucous membrane). With some concentrations of alkali and in some cells a greater swelling is produced by this than by any other chemical except an acid. The less evidence we have of the production of acids in a cell or a tissue used for such experiments as we are describing, the greater do we find the power of alkalies to be in making them swell. When much acid is produced this neutralizes the alkali, so that in the end we get the effect of a low concentration of alkali with much salt (formed through neutralization) against the effect of a stronger alkali with a little salt (that normally found in the cell) upon the swelling of the cell colloids. All the cells mentioned in this paragraph swell less in any salt solution than in distilled water. With every increase in the concentration of the salt there comes a progressive decrease in the amount of the swelling. At a certain concentration the cells maintain for a variable length of time what is considered their "normal" volume. If the concentration is increased beyond this they shrink. In this brief description are exemplified all that is contained in the terms plasmoptysis, turgor, and plasmolysis as understood by the plant physiologists. Impossible as it is to understand all these phenomena on the basis of osmotic pressure, equally easy is it to see in them a perfect

parallel of an emulsion colloid swelling in a dilute acid in the presence of variable amounts of any salt.

The experimental observations on changes in cell volume upon which the just detailed conclusions are based were made by Hamburger in 1887, though they were not published until 1904, because the results did not fit in with the conception of the living cell as an osmotic system which Hamburger, like the plant physiologists, H. De Vries and W. Pfeffer, before him, was most interested in seeing established experimentally. The role of the colloids in accounting for the exceptional behavior of these various cells was, however, considered by Hamburger. Unfortunately he believed the latter a mere adjunct[1] to the biological importance of osmotic pressure, and not, as seems more correct, of *primary* importance—of such importance, in fact, that it not only relegates the role of osmotic pressure to a secondary place, but in most instances, if not all, questions its entire biological significance so far as water absorption is concerned. In a much more positive way has Wolfgang Pauli[2] declared the swelling of white blood corpuscles in dilute acids and alkalies to be analogous to the swelling of colloids under similar conditions.

2. On the Interpretation of Some Experiments on the Absorption of Water by Muscle.

It is well to return for a moment at this point to the interpretation of some of the experiments that were carried out by Jacques Loeb and E. Overton on the absorption of water by muscle. While the experimental results of the two authors agree very well, the explanations that they give of them is very different. As neither of their explanations has found general acceptance on account of the serious objections that can be raised against them, I would like to call attention to the harmonizing explanation that can be given of the observed facts on the basis of the colloidal idea

[1] "Die an der wasseranziehenden Kraft des Zellinhalts wenig betheiligten Colloidtheilchen," Hamburger, Osmotischer Druck und Ionenlehre, Wiesbaden, 1904, iii, 4.

[2] Ergebnisse der Physiologie, 1907, vi, 126 and 127.

of water absorption as already discussed in a previous section of this paper (see Section IV, Part 1) dealing with the absorption of water by muscle.

If a frog's muscle is dropped into distilled water it suffers a progressive increase in weight. This phenomenon is usually interpreted as a response to immersion in a solution of too low an osmotic pressure, so that water is absorbed by the cell contents. I maintain that this is not correct, for were it, all our muscles ought to swell whenever we consume a quantity of fresh or distilled water, and a frog living in a fresh water pond ought to do likewise. But this does not occur. Clearly the muscle swells only because removed from the body.

The difference between the muscle inside and outside of the body is this: Outside of the body the muscle develops an acid reaction, and in this and its effects upon the muscle colloids I would find the cause for the increased absorption in distilled water. Added to this is the effect of the diffusion of salts out of the muscle, for the higher the concentration of salts in an (hydrophilic) emulsion colloid the less does that colloid swell in a dilute acid. Quite contrary to the generally accepted belief, a loss of the osmotically active electrolytes of a tissue may, therefore, distinctly *favor* the absorption of water. We will do well to consider this whenever we try to define wherein lies the "poisonous" effect of distilled water.

That the extirpated muscle becomes acid in reaction must be borne in mind when we try to interpret the effects of acids, alkalies, and salts upon it. To put a muscle into a dilute acid instead of into distilled water is simply to add the effects of the external acid to that produced spontaneously by the muscle. The effect of putting a muscle into an alkali must depend upon the concentration of the acid formed spontaneously in the muscle and the concentration of the added alkali. Depending upon whether the latter partially, entirely, or more than entirely neutralizes the acid formed in the muscle we get as a final result the muscle swelling in a dilute acid plus certain salts, in a neutral solution of certain salts, or in an alkaline solution plus certain

salts. As the amount of acid formed in a muscle is quite variable, and as in consequence the possibility arises of many differently concentrated mixtures of acid, salt, and alkali, we have no difficulty in accounting for the large variation in results obtained when extirpated muscles are placed in dilute alkalies.

Most interesting are the effects obtained when muscles are placed in solutions of various electrolytes or non-electrolytes. Let it again be recalled that the extirpated muscle is not neutral in reaction, and that in consequence its colloids are not absorbing water from a neutral solution. It is really absorbing water from a faintly acid one, so that the problem is really that of a colloid swelling in a dilute acid to which an electrolyte or a non-electrolyte has been added. Let us first consider the electrolytes. Overton expresses surprise that while a 0.6 per cent. sodium chloride solution is in "osmotic" equilibrium with the red blood corpuscles of the frog, the muscle of the same frog demands a 0.7 per cent. solution to keep it from swelling. The explanation is found in this. The muscle rapidly produces acid (within minutes to hours), while the red blood corpuscles do so only very slowly (several hours to days). To counteract the early acidity of the muscle more neutral salt is demanded. The sodium chloride solution that is customarily spoken of as a "physiological," "isosmotic" or "isotonic" salt solution for use with frogs' muscle is, therefore, clearly one that is sufficiently concentrated to just prevent the swelling of the muscle through the production of acid that takes place within it. When now the "isotonicity" of different salts is determined it does not surprise us to find that this is not identical with their "isosmoticity," for the physiological coefficient is not identical with the physical one. On the osmotic conception of water absorption physically "isosmotic" solutions ought to be physiologically "isotonic." Yet experimentally this is not found to be the case. On the colloidal basis of water absorption this result, of course, does not surprise us, for physically isosmotic solutions of different salts are not equally effective in reducing the swelling of an (hydrophilic) emulsion colloid in a dilute acid.

With every increase in the concentration of the salt solution we expect on the colloidal basis of water absorption a decrease in the amount that the muscle swells. This experiment shows it to be the case. As we pass from the "hypotonic" solutions to those considered "isotonic" the muscle swells progressively less. If enough salt is added, the muscle not only does not swell, but shrinks to less than the volume of the freshly extirpated muscle. This marks the progression from the "isotonic" solutions to the "hypertonic." To explain these facts on the osmotic basis, Overton assumes the individual muscle cells to be impermeable to the salt. In the colloidal theory the cells may be freely permeable, which, as a matter of fact, we know physiologically they must be, otherwise it would be impossible to affect the behavior of muscle as markedly as we can experimentally through various electrolytes.

Let us now turn to the non-electrolytes. Overton concludes that the muscle cells are permeable to practically all of these. This conclusion, drawn from the fact that a long series of chemical compounds permit muscle to swell just as though they were not present, is undoubtedly correct, though it is not explained by saying that an osmotic membrane exists about the muscle cells which excludes salts while it is permeable to these non-electrolytes. The extirpated muscle again absorbs water because it grows acid out of the body, and non-electrolytes in contrast to the electrolytes are practically without effect in antagonizing the action of the acid. Let us illustrate these conclusions by citing two of Overton's experiments.

(*a*) A sartorius muscle which has not changed in weight after some hours in a 0.7 per cent. NaCl solution undergoes no change in weight if placed in a solution of 0.7 per cent. NaCl containing 5 per cent. methyl acohol, in spite of the fact that the osmotic pressure of this mixture is equal to a 5.2 per cent. NaCl solution. Overton explains these facts by saying that in a solution of 0.7 per cent. NaCl, the osmotic pressure within and without the cells is the same, and that while the osmotic pressure of the second solution is vastly higher than that of the contents of the muscle

cell, it cannot become effective and withdraw water from the cell, because the methyl alcohol enters almost instantly into the muscle fibers. The correct explanation to my mind is this: The sodium chloride solution has a concentration just sufficient to counteract the effect of the acid formed in the excised muscle, and so maintains the colloids of the tissues in a condition in which their affinity for water suffers no great change in the hours devoted to the experiment. As the non-electrolytes are practically without effect upon this affinity of the colloids for water in the presence of a little acid, an addition of 5 per cent. methyl alcohol to the pure sodium chloride solution does not alter this absorption of water by the muscle.

b) A sartorius muscle which is placed in a solution of 0.5 per cent. NaCl + 3 per cent. methyl alcohol – a solution which has approximately the osmotic pressure of a 3.6 per cent. NaCl solution – gains in weight just as though it had been placed in a pure 0.5 per cent. (a somewhat hypotonic) NaCl solution. If removed to a 0.7 per cent. NaCl solution, the original weight is regained.

Our explanation of these facts reads as follows: The muscle gains in the NaCl-methyl alcohol mixture because the concentration of the NaCl is too low to keep the colloids of the tissues from swelling in consequence of the acid produced in the muscle after removal from the body, and so it absorbs water. The presence of the methyl alcohol is without effect because the non-electrolytes are practically without effect on the swelling of colloids in the presence of an acid. When the muscle is removed to the 0.7 per cent. NaCl solution we encounter a concentration which counteracts the effect of the acid more completely, and since the taking up and giving off of water by colloids represent in large measure reversible processes, the muscle gives up some of its absorbed water and so assumes its original weight.

It is a simple matter, therefore, to account for all the available experimental facts on the absorption of water by muscle on the colloidal basis. Not only are the facts which it has been difficult to harmonize with the osmotic conception of water absorption

explained in this way, but all the phenomena which we have been most willing to accept as osmotic may well represent only a fraction of that greater series of phenomena which we have designated colloidal. The entire question of the validity of the laws of osmotic pressure in the biochemistry of water absorption is therefore raised in the special case of muscle just as we have previously raised it in the case of spermatozoa, isolated epithelial cells, and white blood corpuscles.

That the laws of osmotic pressure, even as rendered more generally applicable to biological material through Overton's special assumptions, are incapable of accounting for all the observed biological phenomena, is admitted by this author himself, and in seeking an explanation of various aberrant phenomena he too considers the role of the tissue colloids. He refers, as Pfeffer before him, to the part played by the imbibition water of the cells (Quellungswasser), and at one point correctly to my mind declares the swelling of muscle in dilute acids to be identical with the swelling of fibrin in dilute acids. But upon this colloidal absorption he does not lay much weight, as is very evident in even his latest writings.[1]

It must be clearly understood that this questioning of the role of osmotic pressure in biological material so far as water absorption is concerned does not question its importance in the general problem of the diffusion of dissolved substances. This is an entirely separate problem. Only our colloidal conception of water absorption renders possible the diffusion of dissolved substances into regions where on the osmotic conceptions we knew they could not get. As already pointed out, neither do our considerations affect the general biological significance of the law of partition as worked out by Hans Meyer and E. Overton in their experimental studies on the cell lipoids.

[1] See, for example, his article in Nagel's Handbuch der Physiologie, 1907, ii, 2 te Halfte, 744 to 896.

3. On the Nature of Hemolysis.

The following are among the most important ways now known to us by which hemolysis (escape of hemoglobin from the red blood corpuscles) may be brought about:

(*a*) Through the addition of water to the blood, or through immersion of the red blood corpuscles in any salt solution having a concentration below a certain value (as ordinarily stated, below the osmotic concentration of the plasma).

(*b*) Through the addition of alkalies.

(*c*) Through the addition of acids.

(*d*) Through the addition of urea and certain other simple chemicals such as alcohol, acetone, and most ammonium salts. Most ammonium salts allow hæmolysis to occur even when present in concentrations at which most other salts do not permit hæmolysis.

(*e*) Through putrefaction of the blood.

(*f*) Through electricity, but only under circumstances which allow of the formation of acids and alkalies in the solutions containing the corpuscles. This paragraph, therefore, constitutes only a subheading of *b* and *c*.

(*g*) Through heating the blood.

(*h*) Through the addition of complex chemical substances, such as saponin, sapotoxin, bile derivatives, and snake venom. With these we must class the specific thermolabile hemolysins.

While hemolysis is easily produced by any of the methods outlined, the following difference is to be observed between the different methods. When a specific hemolysin, or a poison capable of acting at a very low concentration, is added to the blood, the hemoglobin escapes from the corpuscle, but the corpuscle undergoes no change in size. With few exceptions this is not the case in any of the other solutions—in all of them the red blood corpuscles increase in size when the proper concentration at which hemolysis occurs is reached. Especially marked is this in the solutions of acids and alkalies in which hemolysis occurs very rapidly, and in which swelling is most pronounced.

It is not strange after what has been said that a causal connection has been sought between this escape of hemoglobin and the swelling of the corpuscle. In nearly all of the illustrations given, the two processes go hand in hand—it is generally stated that as soon as the red blood corpuscle swells it gives up its hemoglobin. It is not surprising, therefore, that it seemed to several observers as though the only thing necessary toward a complete understanding of the *physical* (not biological) half of the problem of hemolysis was a physico-chemical conception of this process of swelling.

Upon closer study it was found that the salt solutions which just prevent the hemolysis of red blood corpuscles all have very nearly the same osmotic pressure, and so we find the theory advanced that the red blood corpuscles are surrounded by a semipermeable film, and that they swell or shrink, give up their hemoglobin, or do not do so, depending upon whether the surrounding solution has a lower osmotic concentration than the corpuscular contents or the reverse. This conception is a purely mechanical one—as soon as the osmotic concentration of the fluid without the cell is below that of the cell contents, water passes into the cell, which in consequence swells. When this swelling has become sufficiently great, the corpuscle is rent asunder and the hemoglobin escapes.

As the number of experimental observations on the behavior of the red blood corpuscles has increased, more and more facts have come to light which show that the laws of osmotic pressure have only a most limited application to the problem of hemolysis. It is needless to recite all the objections here.

By way of illustration, it is enough to mention that isosmotic solutions of *all* salts and non-electrolytes do not at a certain concentration prevent hemolysis (ammonium salts), that the amount of swelling of the red blood corpuscles in isosmotic solutions of different salts and non-electrolytes is not the same, and that with the same salt the calculated decrease or increase in the volume of the corpuscle is not strictly proportional to the increase or decrease in the osmotic concentration of the surrounding

medium. Certain of these objections have been met, at least in part, through Overton and Meyer's studies on the lipoids. But even with these modifications many of the phenomena observed, notably the action of acids or alkalies, cannot be at all satisfactorily explained on the osmotic basis.

If we call to mind once more the effect of various external conditions on the swelling of fibrin, a ready explanation is obtained of most of the phenomena observed in hemolysis *so far as the changes in the size of the corpuscles is concerned.* Red blood corpuscles (or more correctly put, their stromas) swell most in solutions of acids or alkalies. This is also true of fibrin. The presence of various salts diminishes the amount that red blood corpuscles swell. The same we found to be true of fibrin. Doubling the osmotic concentration of the salt does not halve the volume of the fibrin - the volume remains greater than half the original. Red blood corpuscles behave similarly. When isosmotic solutions are compared, red blood corpuscles are found to swell more in some than in others. We found the same fact to hold for powdered fibrin. All these analogies seem to me to indicate that *the changes in the volume of the red blood corpuscles are dependent primarily upon changes in their colloids.*[1] *Those external conditions which lead to an increased affinity of the colloids for water cause red blood corpuscles to swell, and those which do the reverse, cause the red blood corpuscles to shrink.*

It will be noticed that I have limited myself thus far to a mere discussion of the swelling and shrinkage of the red blood corpuscles, and have connected these processes in no synonymous way with the escape of hemoglobin from the stroma. This is because *I consider changes in the volume of the red blood corpuscles and the loss of hemoglobin by the stroma separate processes, which while they may often be associated, have really nothing to do with each other.* This conclusion is based upon the following facts:

[1] Wolfgang Pauli (Ergebnisse der Physiologie, 1907, vi, 127) seems first to have considered it possible that the absorption of water by colloids and the absorption of water by red blood corpuscles are analogous. He does not discuss the matter of loss of color. More recently Julius Kiss (Periodische System der Elemente und Giftwirkung, Vienna, 1909, only accessible as a book review) comes to the same conclusion. Kiss, however, seems to consider swelling and loss of hemoglobin parallel processes. See above.

When we try to picture the construction of a red blood corpuscle in our minds, these points are of interest: *The red blood corpuscle is essentially a mixture of several colloids.* Of first interest is the protein body which is ordinarily said to constitute the stroma of the red blood corpuscle, and which, from the way it becomes gelatinous in agglutination experiments with red blood corpuscles, has been described as "fibrin-like" in character. Every one of its physico-chemical reactions betray it to be a (hydrophilic) emulsion colloid. Mixed with this stroma are the two lipoids, lecithin and cholesterin. According to R. Höber, the former of these particularly, shows some of the pronounced reactions of the (hydrophilic) emulsion colloids (witness its so-called "myelin reaction"). These two fat-like bodies have, however, a property not possessed by the protein portion of the corpuscle they are good solvents for ether, chloroform, alcohol, and the remaining lipoid-soluble substances. As a fourth important constituent of the red blood corpuscle we have the hemoglobin. This, too, is a colloid, even though most of the hemoglobins can be obtained with varying ease in a crystalline form. A class difference, however, exists between hemoglobin and the other colloids that have been enumerated as contained in the red blood corpuscle. Hemoglobin is not a hydrophilic but a hydrophobic colloid; it is not an *emulsion colloid* (emulsoid) as the protein constituents of the red blood corpuscle, or lecithin, but a *suspension colloid* (suspensoid).

What now is the nature of the combination between the various emulsion colloids (the stroma with the lecithin and cholesterin mixed in) and this colored suspension colloid? Hemoglobin cannot simply be *dissolved* in the red blood corpuscle, for the amount of this coloring matter contained in the corpuscle is entirely too high. Since, for reasons that I have touched upon in the remarks on the biological significance of the analogy between the swelling of (hydrophilic) emulsion colloids and protoplasm, I am no longer able to believe in membranes about cells, either in the form of the simple osmotic conception of semipermeable membranes, or in their modified form as membranes made up

of lipoids, I have, therefore, also to reject the belief that the hemoglobin is simply contained in an oil-covered sac, and that when this is dissolved, or punctured, the hemoglobin flows out. *The hemoglobin must be combined in some more or less fixed way with the rest of the corpuscle. The lack of evidence to show that this combination between stroma and hemoglobin is a chemical one, and the fact that an enormous amount of hemoglobin is held by a very small amount of stroma*[1] *leads me to assume that the combination between the hemoglobin and the rest of the corpuscle represents an adsorption phenomenon.*[2]

I decided to test this hypothesis by constructing a system which simulated red blood corpuscles and then trying the effect of different external conditions upon it. As such a system I used powdered fibrin which had been stained deeply red with neutral carmine. I chose this combination in order to obtain an (hydrophilic) emulsion colloid (fibrin) united with a (hydrophobic) suspension colloid (carmine).[3]

As many, if not most, of the dying processes represent just such combinations between colloids, it would, of course, be an easy matter to choose other hydrophilic colloids, and other dyes, and depending upon their general and their specific properties, obtain results similar to and different from those which I obtained with my carmine stained fibrin. I found, for example, that fibrin stained with hematoxylin behaves very much like that stained with carmine.

I stained the fibrin by placing it in a beaker and covering it with a carmine solution. It is interesting to see how the fibrin absorbs enormous amounts of the dye. One has to add fresh dye time after time to replace that which the fibrin has taken up from the supernatant liquid.

[1] Red blood corpuscles contain from 35 to 45 per cent. solids, of which from 80 to almost 95 per cent. (in man) consists of hemoglobin.

[2] As generally held, this adsorption is a purely physical combination dependent upon the enormous surface presented by the adsorbing material. T. Brailsford Robertson has recently criticised this view and insisted that the combination might be chemical. It does not matter, so far as our argument is concerned, how this discussion is finally settled.

[3] My carmine solution is readily precipitated by salts, and is analyzable under the ultramicroscope.

The retention and loss of color by this carmine-stained fibrin is very similar to, and occurs under the same conditions as, the retention and loss of hemoglobin by the red blood corpuscles. This is readily apparent on comparing the following lettered paragraphs with those given in the earlier pages of this section:

(*a*) If this red stained fibrin is placed in water, the water slowly becomes red. In a solution of sodium chloride, or in the chlorides, bromides, acetates and sulphates of sodium, potassium, or lithium, this loss of color does not occur until after two or more days, when the supernatant liquid may become faintly pink.

(*b* and *c*) If a little of any acid or alkali is added to the colored fibrin, whether suspended in distilled water or in a solution of sodium chloride, the loss of color occurs very promptly. While the colored and powdered fibrin when suspended in a salt solution has an opaque appearance, the bright transparency of a blood that has been laked is suggested after the carmine has come out. Upon standing for a little while the fibrin flakes sink to the bottom of the test-tube, so that the clear, transparent, red solution collects above the swollen uncolored "shadows" of the fibrin particles.

(*d*) Urea at any concentration brings about a prompt loss of color by the carmine stained fibrin. Ethyl and methyl alcohol or glycerine act similarly, but not so powerfully. Solutions of ammonium salts also allow the stained fibrin to lose color in a way that the other salts do not.[1]

(*e*) I allowed some carmine stained fibrin to putrefy in an uncovered dish. As the putrefaction progressed the supernatant liquid became more and more red.

(*f*) The effect of electricity was not studied.

(*g*) Gently heating some carmine-stained fibrin brings about a prompt loss of color.

(*h*) The effect of such substances as saponin, snake venom, etc., has not yet been studied.

The way in which red blood corpuscles lose their hemoglobin

[1] It is, of course, to be foreseen that were the carmine dissolved or adsorbed in a *lipoid*, the effect of the ethyl and methyl alcohols would be much more marked, and so imitate the phenomena observed in hemolysis yet more perfectly.

is not unlike the manner in which carmine-stained fibrin loses its red color in a dilute alkali. As is well known, red blood corpuscles when subjected to a hemolytic agent do not lose their coloring matter suddenly, but progressively. When ordinary blood is mixed with water the hemoglobin ring above the sedimented corpuscles slowly grows a deeper and deeper red. The same occurs with colored fibrin. In this simple fact is found a serious argument against any of the generally accepted mechanical conceptions of hemolysis which only postulate ruptured membranes and the escape of the hemoglobin contained within these membranes. Under such circumstances the escape of hemoglobin would always have to occur more or less suddenly, while we know it to be, as a matter of fact, a progressive affair.

Just as it has been found that an escape of hemoglobin and a change in the size of the red blood corpuscle (the stroma), while frequently associated, do not quantitatively parallel each other, so also can carmine-stained fibrin be made to lose or retain its red color entirely independently of the amount of change in the volume of the fibrin particles. The red fibrin swells enormously and promptly loses its color in a dilute alkali. The higher the concentration of the alkali the more rapidly and completely does the fibrin lose its color, yet so far as the swelling of the fibrin is concerned an optimal point is soon reached beyond which every increase in the concentration of the alkali makes for a diminished absorption of water. Again, if a little ammonium chloride is first added to the alkali, the loss of color is (practically) unaffected, and yet the fibrin swells but little. In other words, the swelling of the colored fibrin follows the laws which Gertrude Moore and I have previously laid down; the loss of color entirely different ones.

It seems to me that this analogy between the loss of hemoglobin by the red blood corpuscles, and the loss of color by carmine stained fibrin is more than accidental, and lends no mean support to the contention that the combination between hemoglobin and stroma is an adsorption phenomenon. If this is granted, then we will have to look for an interpretation of the phenomena

observed in hemolysis into a different chapter of physical chemistry than that into which we have been accustomed to look.

In the model used above upon which to study some of the phenomena of adsorption, I chose an (hydrophilic) emulsion colloid (fibrin) united with a (hydrophobic) suspension colloid (carmine). As already pointed out any other hydrophilic colloid united with any other of the ordinary (colloidal) dyes might just as well have been chosen. We know now that the majority of these dyeing processes represent adsorption phenomena. We know, moreover, how such an adsorption between adsorbing body and adsorbed material may be increased, decreased, or prevented altogether, as witness our use of the most varied mordants, precipitants, fixants, and bleaches. Many of the methods thus employed (the use of salts, acids, bases, formaldehyde, colloids of various kinds, heat, electricity, etc., in the dyeing processes) are found to have a parallel in the list of the ways and means by which the combination between hemoglobin and stroma may be increased or decreased.[1]

The relationships between the different colloids in the case of the red blood corpuscles are, of course, much more complicated than in the case of carmine-colored fibrin. In place of only two colloids, we have in the red blood corpuscles at least four to deal with, and this makes for an infinitely more complicated system. Not only may the individual adsorption characteristics of any group of colloids toward a single other one (hemoglobin in this case) be different, but they may mutually affect each other and so alter each other's adsorption characteristics. Lecithin and cholesterin, for example, have properties which allow them not only to share in, or modify the ordinary adsorption phenomena, as exhibited by the protein constituents of the red blood corpuscles, but through their lipoidal character they may not only absorb substances which the rest of the corpuscle cannot take up, but they may be affected by means which do not affect the rest of the blood corpuscle. Just

[1] Oscar Berghausen showed me in Paul G. Wooley's laboratory, in the University of Cincinnati, an excellent illustration of this. The hemolysis of human red blood corpuscles by carbon dioxide can be markedly inhibited or prevented entirely by the addition of sodium citrate.

in so far as these lipoids affect the relationship of hemoglobin to the protein constituents, or of hemoglobin to themselves, any substance capable of affecting the lipoids (chloroform, ether, acetone, etc.), must be able to influence the whole problem of the relation of the hemoglobin to the rest of the blood corpuscle, and so the problem of hemolysis.

4. On Growth and Some Growth Phenomena.

The *turgor* of plant and animal cells is generally recognized as of such fundamental importance in growth, and in some of the phenomena that are associated with growth, that the following brief remarks, which are merely intended to show how important a role the colloids may play in the whole problem, are perhaps not out of order.

Let us first consider the question of growth in general. As the term has been given various meanings by different authors during the past half century, it is well that we begin with a definition. Least open to objection is that of T. H. Huxley, who speaks of growth as "increase in size." C. B. Davenport defines it more precisely when he regards it as "increase in volume." Objections to all other definitions arise from the fact that in them are too often included those changes which are better considered under the caption "differentiation." These changes, while they may serve as a necessary introduction to, accompaniment of, or consequence of growth, have really nothing to do with the process itself. Driesch's distinction between a "passive" growth due simply to the taking up of water and an "active" growth due to assimilation is excellent, though, as Davenport has pointed out, the term "passive" is poorly chosen, for the taking up of water is by no means a passive process, and that part of growth in which water is absorbed usually gives far more palpable external evidence of its existence than that included under Driesch's heading of "active" growth.[1]

[1] See C. B. Davenport, Experimental Morphology, New York, 1908, 281 to 375.

An objection that we might raise against Huxley and Davenport's definition arises from the fact that not every increase in the volume of a cell, a tissue, or an individual necessarily represents what we ordinarily regard as growth. The development of an œdema in the extremities of an individual, the temporary swelling of a muscle after exercise, the imbibition of water by certain cells of the sensitive plant when touched would all have to be regarded as "growth." In actual practice we would, however, have little difficulty in distinguishing between true growth and the phenomena cited. Perhaps in the end, when the physical analysis of these various physiological and pathological processes is complete, we may find that that which makes these processes overlap in definition makes them overlap in nature also.

The question to which anyone discussing the general problem of growth (increase in volume) is most desirous of getting an answer is this: *What is the source of the energy for growth?* That the energy set free is at times exceedingly great is clearly enough indicated by the every-day evidence of the enormous pressures exerted by the growing tips of roots and stems, and the direct measurements that have been made of the pressures exerted by woods, pulps, and seeds when soaked in water. The greatest osmotic pressures that may be conceived in cells (assuming them, for example, to contain saturated solutions of substances of very low molecular weight) cannot account for more than a fraction of the observed pressures. *The pressures exerted by swelling colloids constitute an adequate source.* We need only to say how under the conditions in nature these pressures are rendered effective. Let it first be called to mind that an absolute *sine qua non* for growth is the presence of water. How necessary is an adequate supply is evidenced by the farmer's worry about rain, and the laboratory experience of every worker in physiological botany. Secondly, all growth in volume is preceded by the production of various (hydrophilic or emulsion) colloids. But not only are various colloids produced, but conditions which particularly favor the absorption of water by these colloids are also instituted. It is the rule, for example, that the growing tips

of plants have an acid reaction; and the role of acids in making various emulsion colloids swell is familiar to us from previous considerations. We have no difficulty now in understanding the observation long familiar to the plant physiologists (to whom we are indebted for most of our knowledge of growth) that there exist in the tips of plants three well-defined regions of growth.[1] At the extreme tip is found a region of rapid cell division with comparatively slow growth. Here is occurring a deposition of colloidal material. Below this is found a region exhibiting great growth. In this but little increase in colloidal material is noted, but the greatest absorption of water. Why such a process should be found to consume much less time than the synthesis of colloidal material in the tip explains itself. The third region again shows little or no increase in volume, but abounds in the changes collectively termed "differentiation." In plant cells a part of this differentiation consists in the formation of cellulose walls. As cellulose constitutes a colloid that is not affected by acids, bases, salts, and various non-electrolytes at concentrations compatible with life, changes in the volume of adult cells (such as growth phenomena) are impossible. Only the colloidal material within the cellulose membrane can be affected by these substances, in consequence of which it may shrink away from the cellulose membrane (plasmolysis) or swell to burst it (plasmoptysis).

The colloidal conception of water absorption also gives us the means of understanding the mechanism of certain *growth curvatures*, and *curvatures due to tropisms* of various kinds as manifested in plants and animals. The remarks that follow apply particularly to plants, in which Sachs first worked out the general problem of the tropisms, though they are just as applicable to many animals whose tropisms Loeb has shown to be identical with those demonstrated by Sachs in plants.

In consequence of the directive action of various external stimuli (light, heat, chemicals, electricity, water) the growing parts of plants bend and grow toward or away from the source of the stimulus (positive and negative tropisms). Growth curvatures

[1] See Davenport, Experimental Morphology, New York, 1908, p. 283.

may also evidence themselves in consequence of differences in the intensity of the action of external stimuli. Various explanations have been given of how these curvatures are brought about. In most the effect of *an increased growth*, as evidenced particularly *through the presence of an increased amount of water* in the convex portion of the plant stem or root, or the animal organism, over that of the convex portion, best explains the observed phenomenon. The question at issue now is how such an increased absorption of water by one side of a stem, for example, is brought about. Osmotic forces have been considered, but they are inadequate from both a qualitative and a quantitative standpoint. The phenomenon is quite easily understood on the basis of the absorption of water by colloids. It is first of all noteworthy that tropic curvatures both in plants and in animals are confined almost strictly to the actively growing parts, and of these particularly to those regions in which we know various emulsion colloids are being produced most energetically (for example the tips of root and stems where synthetic changes are most active). We know, moreover, from the experimental studies of F. Czapek[1] that under the influence of the "stimulus" of a tropism the chemistry of the stimulated protoplasm is entirely different from that of the unstimulated. Between these chemical differences the (hydrophilic) emulsion colloids and an available source of water all the conditions are offered which lead to an inequality in the swelling of the two sides of the vegetable or animal organism, and a consequent turning toward or away from the source of the stimulus. It also becomes intelligible why the older portions of a plant usually take no part in these tropic curvatures. The cells constituting these older portions are surrounded by (colloidal) membranes (such as cellulose) which are not affected by the slight chemical changes (low concentrations of acids, alkalies, and variations in the distribution of various salts) that are capable of affecting so markedly the general body of younger cells and the cells contents of the older ones.[2] Through these more or less

[1] Ber. d. deut. Bot. Gesellsch., 1898, xv, 516.

[2] See, for example, the experiments of Louis Kahlenberg and Rodney True (Botanical Gazette, 1896, xxii, 81) on the effects of acids, alkalies, and salts on growth.

rigid cell walls both the expansion and the contraction of the adult cell is markedly hindered.

Our remarks show the effect of various external stimuli to be due in the last analysis to chemical changes induced in the growing protoplasm, and so the effect of these external conditions on growth come to be referred to just such local chemical changes that we have long recognized as underlying the local irregularities in growth originating within the plant or animal itself. How important in this problem must be the production of different colloids (albumin, glycogen, starch, cellulose, lipoids, with their qualitative and quantitative differences in their affinity for water) in different parts of the growing organism, or, with the same colloid, the localized production of acids, alkalies, and salts is readily apparent. We can also see why, barring specific chemical effects, the action of electrolytes on growth should be so much greater than that of non-electrolytes. Electrolytes affect colloids in a way that non-electrolytes do not.

These ideas on growth can be tested and many of its phenomena mimicked in the laboratory by utilizing a few colloids and various electrolytes and non-electrolytes. Very naturally what must happen in these experiments can be foreseen, though the results are nevertheless interesting. With the use of cylinders, strips and leaves of gelatine various phenomena considered characteristic of the tropisms resulting from the action of chemicals, light, heat, etc., and certain irregularities in growth resulting from internal causes can easily be produced in the laboratory. When such gelatine preparations are painted with a little acid on one side and are then dipped in water beautiful negative curvatures are produced. If acidified gelatine is used and one side is painted with an alkali or a neutral salt, positive curvatures result. Or if a mixture of gelatine with egg albumin is employed a negative curvature results when a weak acid is employed, while a positive results if a stronger one (nitric acid) or a salt capable of coagulating the albumin is applied. When the gelatine has stirred into it, in an irregular way, any dry acid (tartaric, oxalic), and strips are then cut out of this and are moistened with water, complicated

curvatures and irregularities in growth, such as characterize flowers, for example, can easily be obtained.

In conclusion, let attention be called to the ready explanation which the colloidal conception of water absorption offers of the ways and means by which it has been found that certain plants and animals protect themselves from a loss of water. Aside from certain gross advantages of external form, protective covering, etc., it is known that plants possess internal mechanisms by which they protect themselves from a loss of water when this becomes scarce. It is through such mechanisms that the plants of the deserts and the dunes are capable of maintaining their existence. Certain strains of animal and vegetable aquatic life are also possessed of such a mechanism, otherwise they could not withstand the transport from fresh water to sea water, and vice versa. Through the work of van Rysselberghe[1] we have become familiar with the fact that when water is scarce certain plants convert some of their starch into oxalic acid. Those types of plants which under natural conditions are most liable to suffer from lack of water (the succulents) seem all to possess the interesting property of reducing their output of carbon dioxide, while producing at the same time various organic acids as soon as subjected to unfavorable conditions for growth. These phenomena of acid production have been generally interpreted as meaning that by such methods the plant increases the number of soluble molecules in its cell contents and so increases its osmotic pressure. A more correct explanation, it seems to me, is this—through the production of these acids the affinity of the plant colloids for water is increased, so that the agencies operating to rob it of this water are counteracted. A question that awaits an answer in the case of animals is whether a like production of acids is responsible here also for the maintenance of a normal water content, as when a fish, for example, born in fresh water moves out to sea.

The important help that the absorption of water by colloids

[1] Quoted by Höber, Physikalische Chemie d. Zelle u. d. Gewebe, Zweite Auflage, Leipzig, 1906, 63.

can render the general problem of the ways and means by which the movement of sap can be accomplished and maintained, in trees for example, needs no specific comment.

IX. ON THE SECRETION OF URINE.

The wealth of experimental and clinical observations available on the physiology and the pathology of urinary secretion are still in need of a satisfactory unifying explanation. The various theories suggested have not yet found a wide acceptance. The mechanical conceptions first put forward by Bowman and Ludwig have in the course of time been discovered to be inadequate, but it is hard to see how the "physiological" and "vitalistic" theories that have been born more recently help the problem along any. The following paragraphs do not presume to give a complete analysis of the subject, they try, however, to show how the general problem can be broken up into a series of smaller ones. An attempt is made to explain some of these, while others are correlated with problems which still await an answer in physical chemistry.

1. General Remarks on the Structure of the Kidney.

The kidney function shows in common with all secretory systems (1) a secretion obtained through (2) a membrane from (3) a source of some kind. In the case of the kidney these terms are synonymous with urine, kidney parenchyma, and blood. We will for a moment consider these separately from the standpoint of their physico-chemical properties.

1. The urine is essentially a watery solution of various electrolytes and non-electrolytes. At times it may be acid, at other times alkaline in reaction. Under normal circumstances, as it escapes from the uriniferous tubules, it contains so little colloidal material that for our purposes it is negligible. Albumin, mucin, etc., are, of course, present even in normal urine, though in such

small amounts that they escape notice when only our ordinary analytical methods are employed.

2. The membrane through which the urine comes is made up of all the cellular and intercellular elements found between the urine on the one side and the circulating blood on the other. It is simplest to think of this membrane as a covering to a long tube through which the blood flows. From a histological standpoint we know that this covering is very different in different parts of the tube. To start with, the wall (membrane) of this tube consists of a layer of endothelial cells covered by a layer of the cells of Bowman's capsule, the whole joined together by a certain amount of intercellular substance. While the endothelial cells continue throughout the length of the tube the additional covering changes, first to the cells of the convoluted tubules, then to those of the different parts of the loop of Henle, then to those of the second set of convoluted tubules, and finally to the cells of the collecting tubules. With all these different cells we must always in our considerations count the intercellular substance that binds them together.

From a physico-chemical standpoint this tube, or, as we had best now call it, this membrane, is colloidal in constitution. It is made up in the main of a mixture of various (hydrophilic) emulsion colloids. But in no sense are the different portions of the tube made up of exactly the same colloidal material either in a chemical or a physical sense. We know this to be true because the different parts of the living kidney take up dyes, for example, with very different avidities when these are injected into the circulating blood. This fact suggests that the different parts of the tube may have different physiological activities.

We have now to point out that while the colloidal membranes with which we busy ourselves in the laboratory are made up of *dead* material, that separating the urine from the blood is *alive*. This does not imply, however, that we must at once become vitalists. It only means that it introduces a series of more or less independent chemical and physico-chemical reactions into our general problem of secretion which demand additional care

and study to analyze. The physico-chemical state of this living membrane is dependent upon the chemical changes that occur in the cells constituting this membrane, and these chemical changes are in turn intimately connected with the changes that occur in the blood supplying these cells. It is readily apparent, therefore, that the introduction of a single variable into the circulation may upset the entire chemistry of the cells of the secreting membrane, and so their physico-chemical state. This is why what looks like such a small change in our entire secretory system may be followed by a most profound effect upon the secretion of the urine both from a quantitative and a qualitative standpoint.

3. The blood represents a mixture of various formed elements with a liquid menstruum. The formed elements are colloidal bodies (nucleated and non-nucleated cells) which react toward changes in their environment (acid, alkalies, salts, non-electrolytes, etc.), in the very definite ways already described. The liquid portion of the blood (the plasma) is a colloidal solution of various proteins. Mixed with this solution are normally a number of different salts and varying amounts of different non-electrolytes.

2. A Model Illustrating Some Phases of Urinary Secretion.

Before continuing our main argument it is well to digress here and to describe a somewhat crude but quite efficient *model of urinary secretion*. Familiarity with it may help to a better understanding of what follows. This model consists of nothing but a layer of very finely powdered (preferably faintly acid) blood fibrin in the bottom of an ordinary calcium chloride tube, the outlet of which has been plugged with a little cotton to keep the fibrin from falling through. The whole is fastened in an upright position into a support. Above it is clamped a large separator funnel furnished with a stopcock which permits regulation of outflow in such a way that a constant level may be maintained in the calcium chloride tube over long periods of time.

If now a "physiological" salt solution ($\frac{1}{2}$ molecular NaCl) is allowed to flow into the calcium chloride tube in such a way

as to maintain a constant level, it is seen to pass through the fibrin (which swells somewhat) and to escape in drops at the lower end of the tube. The rate at which the salt solution escapes (c.c. in units of time) remains constant for indefinite periods of time if the pressure remains the same. If the level of the solution in the calcium chloride tube is raised, then the "secretion" occurs more rapidly.

If in a given model we note carefully the rate at which a sodium chloride solution escapes below, and then substitute an equimolecular solution of sodium sulphate, sodium citrate, or any of the other "saline diuretics," we find that these all pass through much more rapidly than the sodium chloride.

When a dilute acid or a sodium chloride solution containing an acid is substituted for a pure sodium chloride solution, the rate of outflow is seen to gradually diminish, and may finally stop entirely. At the same time the fibrin is seen to swell and the solution that drips through gives an albumin ring with nitric acid. If the pure sodium chloride solution is returned to, or enough of this salt, or better, sodium citrate, tartrate, or sulphate is added to the acid solution, the secretion can be made to recommence, first slowly, then more rapidly, and ultimately the normal, or even a better flow may be obtained. At the same time the albumin ring is found to disappear from the liquid that passes through.

If various non-electrolytes (ethyl or methyl alcohol, urea, glycerine) are used in place of the various salt solutions, either alone, or in combination with an acid, the changes in the rate of outflow are not noted.

The interpretation of these simple facts offers no particular difficulties. The liquids introduced into the calcium chloride tube escape below after traversing a capillary bed formed by a (hydrophilic) emulsion colloid. An increased pressure makes for an increased secretion, as does also any salt capable of making the particles of powdered fibrin shrink, whereby the size of the capillaries is increased. Acids of various kinds which make the fibrin swell have an opposite effect. The antagonism between

neutral salts and acids on the swelling of fibrin explains why such salts as the citrate, sulphate, and tartrate of sodium can make a layer of fibrin permeable to water once more, after it has been rendered impermeable by a pure acid. Albumin appears in the filtrate when it does because the fibrin is (pseudo-) soluble in acid solutions. It becomes less in amount or disappears entirely when enough of different salts is added, because these reduce the "solubility" in acids.

The question now arises whether this model of secretion has anything in common with the physiological and the pathological secretion of urine. I believe it has, though not quite in as coarse a form as the rough analogy between this model and certain phases of urinary secretion might at first suggest. The model here described was, as a matter of fact, constructed to give tangible evidence to conceptions of urinary secretion which a study of the literature and my own experiments had led me to construct in my mind. Just how far I think this model simulates conditions as observed in experiments on the kidneys will appear in the further discussion.

We will take up now a series of experimental findings on the secretion of urine which it seems to me can be interpreted, in the light of our knowledge regarding colloids, in a different and simpler way than is generally done. Our discussion will deal almost entirely with the subject of the secretion of water by the kidneys, and but little with the secretion of substances dissolved in the water. Some writers in physiology and pathology to this day look upon the two as parallel processes. As a matter of fact, they constitute separate problems, and should be dealt with separately.

3. The Secretion of Water by the Kidney.

(*a*) It follows as a necessary conclusion from the argument which has been the burden of this paper, that *in the resting state the living organism represents a series of different (hydrophilic)*

emulsion colloids saturated with water. That they are saturated is evidenced by the fact that we cannot make the organism as a whole absorb any more water or give up any without antecedent chemical changes. In consequence, an organism not subject to any marked changes from without or within maintains a constant weight over long periods of time. We need but recall how all the secretions of a man undergoing absolute starvation drop to practically nothing, and how, on the other hand, the consumption of even enormous amounts of water by the normal individual does not lead to the development of the slightest œdema. We are accustomed to say that the kidneys quickly rid the body of any excess of water. Just why this is done is not so apparent, though we will suggest an explanation right away. Let it first be pointed out that *the blood and lymph constitute an integral part of this water-saturated colloidal system* which makes up the body. It may at first sight seem somewhat surprising that the relation between the colloids and the water of liquid (hydrophilic) colloidal solutions (sols) is identical with that of the relation existing between water and solid colloids (gels) such as fibrin. But such an identity is not only demanded by theory but has been proved experimentally by the recent work of Wolfgang Pauli and Hans Handovsky[1] on blood serum.

We are not surprised to find that the secretion of urine ceases (practically) during absolute starvation. If the colloids of the body as a whole are saturated with water, none is left over to be secreted. Only in so far as the tissues undergo gradual consumption during the process of starvation or their colloids suffer changes which decrease their affinity for water is any liberated to become available for secretion. On the other hand, if a non-thirsting organism (as I will, for short, call an organism whose colloids are saturated with water) consumes a quantity of water, we find that after a variable length of time an amount of urine is excreted which is equivalent to the amount of water that was drunk. (Not to do so means the development of an œdema.) It does not

[1] Biochemische Zeitschr., 1909, xviii, 340.

matter how this water was consumed. It may simply have been swallowed or have been experimentally introduced into the gastro-intestinal tract, or it may have been injected into the peritoneal cavity, under the skin, or directly into the blood. But let it be noted that the water diuresis occurs only in proportion to the amount of "free" water that has been introduced; in other words, water not combined with a colloid. According to our theoretical considerations on the colloids it would be expected that were a (with water saturated hydrophilic) colloidal solution introduced into the vascular system, *no* increased urinary secretion ought to result. As a matter of fact, it does not, as is proved by the old experiments of Ponfick[1] and the more recent ones of Magnus,[2] both of whom found that the injection of blood serum or blood into dogs and rabbits is *not* followed by a diuresis.

The simple fact that an amount of urine is always excreted under physiological conditions equivalent to the amount of water consumed tells us nothing, however, of the mechanism by which this is accomplished. To limit ourselves again to the most physiological of the above conditions, let us try to discover how on the colloidal basis of water absorption, water is always absorbed from the gastro-intestinal tract, and always excreted by the kidneys. We can take a step toward the answer to this question by pointing out that *the anatomical and physiological conditions existing normally in the body tend to keep the colloids of the gastro-intestinal tract and the blood and lymph streams passing through it in an unsaturated condition so far as water is concerned, while the reverse conditions hold for the kidney.* The mouth and œsophagus play practically no role in the absorption of water. The stomach, according to von Mering's experiments, also takes but little if any part in the absorption of water. The small and large intestine are the absorptive organs for this substance par excellence. The stomach is richly supplied with arterial blood. The small and large intestine are also generously supplied, but not as generously as the stomach. The separate

[1] Virchow's Archiv, 1875, lxii, 277.
[2] Arch. f. exp. Path. u. Pharm., 1901, xlv, 210.

branches of the mesenteric arteries which go to supply the villi occupy a fairly central position in this structure and break up into a capillary network which lies close under the intestinal epithelium. As clearly evidenced by the dark color of the portal blood, and direct gas analysis, the blood returning from the intestine is intensely venous (poor in oxygen and rich in CO_2). *This high carbon dioxide content of the blood returning from the intestinal tract increases the affinity of the colloids of the blood for water in consequence of which they absorb it through the intestinal mucosa from the lumen of the intestine as long as it is present there.* The experiments of von Limbeck, Gürber, and Hamburger[1] show that under the influence of such an increase in CO_2 concentration as exists *normally* in venous blood over arterial blood the red and white corpuscles absorb an amount of water which easily amounts to from 5 to over 15 per cent.[2] of their volume in arterial blood. If we use only the lower of these values and ignore entirely the water carrying power of the colloids contained in the plasma, a little calculation shows that a liter of blood passing through the intestinal tract is capable of absorbing 17.5 c.c. of water, for the corpuscles when moist make up in round numbers about 35 per cent. of the blood. Even these values, which have been chosen as low as possible, easily suffice to account for the absorption of great amounts of water from the gastro-intestinal tract.

It requires no special explanation when we say that *the reverse of all these conditions hold when the kidneys are reached.* In its transit through the lungs the venous blood loses the carbon dioxide responsible for the increased affinity of its colloids for water. When, now, the arterial blood reaches the kidneys—which, let it be noted, are supplied with extra large arteries—more water is contained in the blood than the blood colloids are capable of

[1] H. J. Hamburger, Osmotischer Druck u. Ionenlehre, Wiesbaden, 1902, i, 291; ibid., 404.

[2] These figures are nearly doubled if instead of comparing the sizes of the corpuscles in arterial and in *ordinary* venous blood the sizes in arterial and *passively congested* venous blood are compared. In other words, the same circumstances that make the passively congested *organ* become œdematous make the corpuscles *in the blood* become "œdematous."

holding, and so this separates off as urine.[1] These considerations show *why* a water absorption is the rule in the intestine and a water secretion the rule in the kidney. *How* under the influence of an acid the absorption of water by any colloid is accomplished constitutes a separate question,[2] as does also that subsidiary one of *how* the separation of the unbound water through the (colloidal) urinary membrane is effected.

b) The secretion of urine by the kidney is dependent in a very striking way upon *the circulation*. Not only can the "normal" secretion of urine be increased through changes in the circulation, but it can still more strikingly be decreased. From histological studies, and, on the whole, very hypothetical reasonings, W. Bowman (1842) first laid stress on the importance of the *pressure* under which the blood flows through the kidneys as a factor in determining the secretion of urine. This pressure idea was further developed and given an experimental basis by Carl Ludwig (1844) and his pupils. Through their work considerable evidence was advanced to show that changes in blood pressure, no matter how induced, are always followed by changes in the amount of urine secreted, and, on the whole, in this sense, that an increase in blood pressure is accompanied by an increased urinary secretion, while a decrease in blood pressure is followed by an opposite result. This long-accepted belief met a serious setback in the critical studies of R. Heidenhain.[3] Heidenhain showed very clearly that the parallelism between blood pressure and urinary secretion is by no means absolute. Not only does interference with the outflow of venous blood from the kidney—a condition associated with an increase rather than any decrease in blood pressure—lead to a fall in the amount of urine secreted easily equal to the fall encountered after interference with the arterial

[1] The question that naturally arises is why the secretion of water does not occur into the lungs (where the CO_2 escapes) instead of through the kidneys. The reason may be twofold. The colloidal membrane between blood and alveolus may not be freely permeable to water (just as the urinary membrane is not in acute parenchymatous nephritis—see below) or the time necessary for a reversal of the water absorption may be greater than the time the blood spends in traversing the lung capillaries.

[2] See the theoretical considerations of Wolfgang Pauli and Hans Handovsky, Biochem. Zeitschr, 1909, xviii, 353.

[3] Hermann's Handbuch d. Physiologie, Leipzig, 1883, v, 309.

influx of blood, but various diuretics which do not alter the blood pressure are known to bring about a decided increase in urinary secretion. Heidenhain showed very clearly that the experimental facts available in his day are best harmonized by saying that the *velocity* with which the blood passes through the kidney determines the amount of the urinary secretion. But further than this he does not go with any mechanical or, to put it more generally, physico-chemical conception of urinary secretion. In the end he makes this a "vital" process by believing that the epithelial cells of the glomeruli actively take up water and salts from the blood and secrete them into Bowman's capsule. As this salt solution passes down the uriniferous tubules there is secreted into it, again through the "vital" activities of the cells lining the uriniferous tubules, the various substances (urea, uric acid, etc.) that characterize the urine.

In place of the teaching of Ludwig that a secretion of urine is primarily dependent upon a blood pressure, or Heidenhain's belief that the velocity with which the blood passes through the kidneys is of primary importance, I venture to suggest, in interpretation of the experiments and clinical observations at hand on this subject, that *the normal urinary secretion is absolutely dependent upon an adequate oxygen supply to the cells constituting the parenchyma of the kidney. Any interference with this oxygen supply leads to a decrease in urinary secretion even to the point of absolute and permanent stoppage. Through a particularly favorable oxygen supply to the kidneys the secretion of urine may be increased above that ordinarily considered "normal."*

This interpretation meets with no experimental objections. Nature has seen to it that the kidneys shall not lack facilities for a plentiful supply of oxygenated blood by supplying them with strikingly large renal arteries. Any considerable interference with the oxygen supply to the kidney is followed by a drop in urinary secretion. It does not matter how such an interference is brought about. It may be brought about through a change in the action of the heart itself, such as a decrease either in the number or the force of the heart's contractions or both

vagus stimulation, myocarditis, valvular heart disease, dilatation). Or the deficiency in oxygen supply to the kidneys may be brought about through hemorrhage or through stimulation of vasomotor nerves whose effect tends in the aggregate to decrease the amount of oxygenated blood passing through the kidneys. Most effectively can the oxygen supply to the kidneys be diminished to any degree or be cut off entirely through compression of the renal artery from without (experimental ligature or clamp, tumor) or occlusion from within (arteriosclerosis, experimental or clinical embolism). The same result is accomplished if the outflow of blood through the renal veins is sufficiently impeded (experimental ligature, tumor, passive congestion due to heart disease).

An adequate oxygen supply to the kidney, on the other hand, favors the secretion of urine. This is evidenced by the fact that the removal of the various conditions outlined above (provided they have not acted too long) is followed by a reëstablishment of the urinary secretion to normal. When special efforts are made to increase the oxygen supply to the kidneys, as by ligating several of the larger arteries that pass off the aorta, or by stimulating vasomotor nerves which tend to increase the quantity of oxygenated blood passing through the kidneys, a secretion of urine in excess of that considered normal may be obtained. As final proof that the available oxygen carried by the blood (and lack of CO_2) are the important elements in the interpretation of all these experimental findings, we need only recall how the most liberal supply of poorly oxygenated blood to the kidneys, or one that is rich in carbon dioxide, even without any other disturbances in circulation (such as variations in blood pressure), is incapable of maintaining a normal secretion of urine for even a little while.

These paragraphs show how a series of most dissimilar disturbances in the circulation to the kidneys are in effect all the same. We have to say now what is the change wrought in the kidneys through this lack of oxygen. This is a question that we have argued many times before. Through any interference with the oxygen supply to a part we expect an abnormal accumulation

and production of various acids in the affected tissues. Added to this is an abnormal accumulation of carbon dioxide, for the conditions leading to lack of oxygen usually have associated with them the conditions which make for an accumulation of CO_2. Since the tissues contain various (hydrophilic) emulsion colloids we may expect these to swell if only a source of water is present. It is not surprising, therefore, that oncometric measurements have shown that *every interference with the normal blood supply to the kidneys is followed by an enlargement of the organ, independently of any increase in size that may be due to more filling of the vessels with blood.*[1] No further comment is necessary to show how these observations on urinary secretion and our previously detailed experiments on the œdema of passively congested parenchymatous organs dovetail (see Section VII, Part 5).

When the oxygen supply to a kidney is cut off sufficiently, albumin, and at times blood, appears in the urine. Such an albuminuria and hematuria may be made to subside if the condition leading to the lack of oxygen is removed after not too long a time. When, now, we add to these facts of changes in circulation, increase in the size of the kidneys, progressive diminution in urinary secretion to the point of absolute stoppage, albuminuria, and hematuria, the further fact that on section the kidney parenchyma appears swollen, grayish, and with kidney markings obscured, we have no difficulty in recognizing that *we are dealing with a series of changes that characterize the ordinary acute parenchymatous nephritis.* The reason why this fact is brought out here is because the changes that occur in these experimentally induced nephritides are in part analyzable, and so help not only toward a theoretical understanding of what is observed in clinical cases of acute nephritis, but in doing so give promise of being of possible practical worth. They give us, first of all, a coördinated understanding of the origin of the albuminurias that go

[1] See Gottlieb and Magnus, Arch. f. exp. Path. u. Pharm., 1901, xlv, 223. The earlier contradictory results of Starling are open to question. Starling, Jour. of Physiology, 1899, xxiv, 317.

with heart disease, arteriosclerosis, and various other pathological conditions of the circulatory system. Secondly, they suggest that the old argument as to whether primarily bloodvessel changes lead to nephritis, or nephritis leads to bloodvessel changes, is probably best settled in favor of the former. Just what we think regarding these various conditions means much for the theory of our treatment.

Our considerations lead to yet other conclusions. The lack of oxygen induced in the kidneys through circulatory disturbances makes itself felt in the end in the oxidation chemistry of the kidney cells themselves. Now various chemical means are at our disposal by which we can interfere with the oxidations that occur normally in the kidney parenchyma without in any way altering the circulation of the kidney itself. We need mention only the effect of uranyl nitrate and various other metallic poisons, amyl nitrite, the cyanides, and in lesser degree the various anesthetics, such as morphine, chloroform, and ether. Every member of this list, which with varying degrees of ease is known to lead to albuminuria, hematuria, partial or complete suppression of urine, enlargement of the kidney, and various "degenerative" changes in this organ considered characteristic of "nephritis" is known to interfere with the normal oxidations occurring in living tissues. The bearing that all these remarks have on a large number of nephritides, encountered clinically, is apparent not only from the fact that almost every one of the poisons here mentioned has been known to lead to nephritis in man, but by the additional fact that the "toxic" nephritides that appear in the course of various acute infections also belong to this group.

Let me here digress to indicate how a toxic nephritis may add circulatory disturbances to itself and so further aggravate an already precarious condition in the kidneys. The initial toxic disturbance in the kidneys leads to a lack of oxygen in the cells wherein then accumulate various acids which in turn make the kidneys swell. Such a swelling of the kidney cells tends to compress the bloodvessels passing through the kidneys, wherefore a state of lack of oxygen from this source is added to that already

existing. In this connection the fact should be recalled that the capsule of the kidney is not as expansile as the rest of the kidney tissues. *This fact enables us to understand why in at least some cases of acute suppression of the urine (acute nephritis) a stripping of the capsule offers relief of the symptoms.* This procedure tends to restore a normal flow of blood through the kidneys and so not only gives these organs a much needed oxygen supply, but an opportunity for the removal of the toxic conditions primarily responsible for the change in the kidney cells.

In the earlier pages of this paper we became acquainted with the antagonistic effect of various neutral salts on the absorption of water by (hydrophilic) emulsion colloids in the presence of a dilute acid, and later we saw how various salts will reduce the most varied types of local and generalized œdemas. The practice is an old one which administers various salts, particularly of the saline cathartic group, to cases of acute nephritis in order to increase the output of urine. Just how their action is to be interpreted is discussed in detail in the succeeding paragraph (*c*). Here let me point out that one of the effects of giving these salts is to decrease the volume of the kidney.

As the relief of the particularly *acute forms of nephritis* still presents many clinical difficulties, I have tried to discover if some help might not be obtained from the ideas advanced in this paper. The anuria is probably one of the most striking symptoms of the more intense grades of parenchymatous nephritis that are observed clinically. Such an anuria is obtained in rabbits and dogs with the greatest ease if only the renal artery is clamped for a little while. If the clamp is kept in place even a couple of minutes, a fall in urinary secretion is strikingly apparent for some time afterward, and if left in place long enough a secretion from the insulted kidney may never again be obtained. *The coincident swelling of the kidney in these experiments is promptly relieved by direct injection of various salts (sodium phosphate, sodium sulphate, sodium chloride) either directly into the body of the kidney itself, or into the renal artery or into the general circulation.* Most interesting, however, is the fact that *a kidney which under ordinary*

circumstances would never again secrete any urine will do so if these salts are injected. Of the clinical applications that may be made of these facts, as well as detailed experimental findings, I shall speak as soon as a present unavoidable interruption in my work has passed.

(c) We became familiar above with the fact that the presence of "free" water in the blood—that is to say, water present in the blood above the amount necessary to saturate the colloids of the blood under existing conditions—leads to an increase in urinary secretion, and that, other things remaining unaltered, the amount of this increase is proportional to the amount of water that is present in the blood as this passes through the kidneys. We will now consider some further changes in the blood that are associated with variations in the amount of urine secreted, and see how the facts are to be interpreted on the basis of our colloidal conceptions.

The discussion is best begun by considering the *reduction* in urinary secretion that follows the administration of various drugs. It is a familiar fact that after the administration of morphine, chloroform, ether, or alcohol, in any considerable amounts, there is always a fall in urinary secretion that may at times amount to complete suppression. I have already pointed out how all these substances may lead to such a suppression through action upon the kidneys alone. Under ordinary circumstances such a purely local action is, however, not to be anticipated, and it is perfectly conceivable how a temporary suppression of urine might follow, say, a general anesthetic, without any changes in the kidneys themselves. *The administration of all these anesthetics (and various alkaloids) is accompanied by such a state of lack of oxygen in the tissues of the body generally,* as we have before described for isolated organs. In consequence of this the affinity for water of the colloids of all the tissues of the body (including the blood and the lymph) is increased above that considered normal. After administration of any of these drugs *the body generally, therefore, is holding on to its water with special avidity, so that none is left over to be free in the blood and so be excreted through the kidneys.* This condition

of the tissues after an anesthetic or a dose of morphine, for example, is evidenced not only by the lack of urinary secretion, but by the thirst complained of by the patient. As the patient gets over his anesthetic his urinary secretion not only comes up, but his thirst disappears, even though no water has been given. To get the described results it will be remembered that considerable amounts of these various drugs have to be administered. Such doses lead to a state of lack of oxygen in the tissues. *Small* doses of ether, alcohol, etc., *increase* the urinary output. In trying to say how this effect is brought about we have to remember the favorable conditions for secretion that are induced in the kidneys when these are given plenty of oxygen, while at the same time their carbon dioxide is being rapidly carried away. Such conditions are brought about through the increased frequency and force of the heart beat, the more rapid breathing and the vasodilatation that are induced by *small* doses of these drugs. A large part of the diuretic action of caffeine and of digitalis can also be understood on this basis. The drugs which make for an increased oxygen supply and a favored carbon dioxide removal from the kidneys do the same for the body tissues generally. A *decreased* affinity of the body colloids generally for water is, therefore, a natural result under such circumstances, in consequence of which water is liberated into the blood. This water then becomes available for urine. A dose of caffeine or digitalis, therefore, not only puts the kidneys into a condition which favors the secretion of water by them, but at the same time aids in furnishing this water through an indirect effect upon the body colloids generally.

Let us turn now to the consideration of the results that have been obtained when various salt solutions have been injected directly into the blood. When a ("physiological") 0.9 per cent. sodium chloride solution is injected into a rabbit a secretion of urine is obtained which very quickly equals the amount of salt solution infused. If a somewhat stronger salt solution is employed, more urine is secreted than is infused, and this difference between amount injected and amount excreted becomes the greater the higher the concentration of the sodium chloride in the injection

fluid. If the injections are very large, or are carried on for a long time, the *absolute* differences between amount infused and amount secreted remain, but the *relative* become less and less apparent.[1] If no time limits are set upon the experiment, the end results become somewhat complicated (though not confusing), owing to the fact that the animal develops the symptoms and signs of a general œdema. This œdema is due to the lack of oxygen from which the animal suffers whenever these great injections of salt solution are continued sufficiently long.

Isosmotic solutions of the chlorides, bromides, and iodides of sodium or potassium bring about approximately the same excretion of urine.[2] When, however, equally concentrated solutions of the various saline diuretics (phosphate, sulphate, tartrate or citrate of sodium) are injected, a much greater secretion of urine is obtained.[3]

How now are these various experimental findings to be interpreted? Let us first call attention to the important experimental error that is introduced into any of these experiments with salt infusion if any anesthetic is used. When enough is used to produce anesthesia, a lack of oxygen in the tissues and a retention of some of the liquid infused may be expected to follow. The effect of an infusion is divisible into two parts: first, the effect of the water injected, second, the effect of the salt. Other things being equal, we may expect the water to behave, so far as diuresis is concerned, just as this behaves when water only is injected. The salt injected has an effect upon the kidney and also upon the colloids of the body generally, including those of the blood and lymph. As the chief salt of the body fluids is sodium chloride, we are not surprised to find that a sodium chloride solution isosmotic with the blood, when injected intravenously, acts about as the injection of an equal amount of water (the minor effects of pure water as a plasmolyzing agent on the blood, etc., not being

[1] See Martin H. Fischer, University of California Publications, Physiology, 1904, i, 107.

[2] Von Limbeck, Archiv f. exp. Path. u. Pharm., 1888, xxv, 89.

[3] Magnus, Archiv f. exp. Path. u. Pharm., 1900, xliv, 68 and 396; Ueber Diurese, Heidelberg, 1900; Torald Sollman, Arch. f. exp. Path. u. Pharm., 1901, xlvi, 13; B. Haake and K. Spiro, Hofmeister's Beiträge, 1902, ii, 149.

taken into consideration). If, however, a sodium chloride solution having an osmotic concentration above that of the blood is used, an increased secretion of urine is obtained. This is because the salt acts not only directly upon the colloids of the blood and makes them liberate some of their water, but diffuses into the tissues of the body and makes the colloids here also give up a part of their water. This water is then "free," and can be secreted as urine. The salt also acts upon the colloids of the kidney, making the cells of this organ shrink. This shrinkage of the kidney cells necessarily means a change in the physical constitution of the previously described colloidal membrane that separates the urine from the blood. We can say that this change makes for an "increased permeability" of the membrane, but the real physics that underlies this designation cannot yet be satisfactorily gone into. The higher the concentration of the injected salt the more water must the body tissues yield up for diuresis (and the more "permeable," perhaps, also may we consider the kidney membrane to become to water).

We have no difficulty in understanding why isosmotic solutions of different salts are not equally effective in producing a diuresis. We have become familiar with the unequal effects of different salts on the absorption and secretion of water by colloids. Just as the sulphate, tartrate, phosphate, and citrate of sodium are more effective in making fibrin or gelatine give up their water than the chloride, bromide, and iodide of this same metal, so are the former group expected to make the body colloids yield up a greater amount of water for diuresis than the latter. A similar difference of effect is to be expected upon the colloids constituting the membrane separating the urine from the blood in the kidney. The first-named group must tend to make this "shrink" more than the second, whence may come the increased permeability to water.

These considerations can easily be tested by simply reversing our process of reasoning from fact to theory. Let us see how well our theory will fare if we apply it to any carefully worked-out series of experiments on urinary secretion. I have chosen

Ernst Frey's[1] recent findings for such a test. This author does not, of course, interpret his experiments as I have taken the liberty of doing for him, but on the more generally accepted basis of alterations in the kidney and its circulation.

Frey finds that when water is given a rabbit by mouth or rectum, or is injected intraperitoneally or into the small intestine, an increased amount of urine is secreted by the kidneys. I would say that this is because the tissues of the rabbit are saturated with water and so none of it is retained. If in place of water a sodium chloride solution is injected, the same or even a greater diuresis is obtained. This diuresis is the greater the higher the concentration of the salt solution injected (the amount of fluid injected being the same), just as in the experiments of my own already described.

The diuresis following the introduction of water does not occur if any anesthetic is administered (morphine, chloral, ether, urethane). This is evidently because the anesthetics all produce a state of lack of oxygen, so that the tissues have an increased affinity for water and so do not secrete that which has been absorbed from the alimentary tract or peritoneum. Let Frey's finding be noted that these anesthetics do not interfere with the *absorption* of water from the gastro-intestinal tract. We are not surprised in the face of our explanation to note that Frey found this retention of water to occur just the same whether he had previously bled the animal or had cut the nerves to the kidneys, or changed the posture of the animal. Not even when he gave phloridzin or salicylic acid in an attempt to "stimulate" the kidneys did he get a urinary flow. According to our ideas of urinary secretion such a result is entirely to be expected. None of these procedures affect the affinity of the colloids of the tissues for water except as some *increase* it.

The continuance of an absorption of water from the gastro-intestinal tract while none was being secreted through the kidneys is easily explained by the increased affinity of the colloids of the

[1] Pflüger's Archiv, 1907, cxx, 66 to 136 (three papers).

tissues generally for water. On this basis it is also an easy matter to explain the increased absorption of salt solution from the peritoneal cavity in nephrectomized animals, as observed by S. J. Meltzer and Salant.[1] The retention of substances that should be secreted through the kidneys poisons the tissues and increases the affinity of their colloids for water.

The analogies between these various experimental facts on the secretion of urine, and the model previously described and constructed with a view to elucidating some of these facts need no special comment. In our model we have eliminated the colloids of the blood stream, and a colloidal reservoir of water corresponding with the water-saturated body colloids by working with simple salt solutions only. As our considerations have shown, the colloids of the blood and of the tissues generally play a part in urinary secretion only in so far as they furnish storage places for water which is liberated under the conditions employed in the described experiments on diuresis. Our model, therefore, illustrates particularly the changes that occur in the kidney (which represents physicochemically only a much folded colloidal membrane). In our model the "secretion" of "urine" is induced through a hydrostatic pressure which forces a liquid through the capillary bed formed by the powdered fibrin. When an acid is brought in contact with the fibrin it swells, closes the capillary pores, and in proportion to the amount of this closure a formerly effective hydrostatic pressure becomes less and less capable, or, finally, even entirely incapable of forcing any liquid through this bed. We can counteract the effect of this acid by various salts, wherein again we find the saline diuretics to be more effective than certain other common salts. Such a salt as sodium sulphate, of course, makes the fibrin shrink more than an equally concentrated sodium chloride, and so the former, by increasing the size of the capillary pores, more than the latter favors an increased "secretion" in our model. Matters in the living kidney are, of course, not so simple as in this model. To mere changes in hydrostatic (blood)

[1] American Medicine, 1904, viii, 194.

pressure, per se, I think but little significance can be attached. Enormous pressures (not such as we encounter in the body) are needed to filter liquids through even very thin colloidal membranes. In the changes in the surface tension of liquids we deal with more adequate forces.[1] Nor would I be understood as of the opinion that the colloidal membrane constituting the kidney is grossly capillary in character as is our powdered fibrin. But in an analogous behavior of the so-called "microcapillary" character of the colloidal membrane separating the urine from blood I feel quite confident that the solution of our problem lies.

4. The Secretion of Dissolved Substances by the Kidney.

We will enter into the problem of *the secretion of dissolved substances* only sufficiently to point out the illuminating touch given it by the physical chemistry of the colloids. Great pessimism still reigns regarding our ultimate ability to explain, on a purely physico-chemical basis, all the phenomena of secretion. That such a view is not justified must appear from even the brief remarks that follow.

What has been most difficult to explain in secretion has been its selective character; in other words, the ability of the kidney to separate from the blood a liquid which has a totally different quantitative and qualitative composition. *Qualitative* differences are for the most part explainable through chemical changes that occur in the secretory cells themselves, whereby substances are produced (such as mucin for example) which do not appear in the blood at all. In other respects a secretion differs only in quantitative composition from the blood. This may go to the point of having entirely absent from a secretion certain constituents of the blood, as, for example, albumin from the urine. For the most part, however, the secretion contains some substances in higher,

[1] While I do not feel that the ideas of L. Traube on this subject are entirely satisfactory in detail, his general conceptions of the role of surface tension in secretion strike me as most suggestive and valuable.

others in lower concentration than the blood. To limit ourselves again to the urine, we need by way of illustration only recall that, under ordinary circumstances, the urine contains less chlorides than the blood, and more sulphates and urea. How are such differences to be explained?

To begin with, it is well to call to mind that a secretion of dissolved substances is possible only so long as water is furnished the living organism. *A secretion of water is necessary before we can hope to have any secretion of dissolved substances.* This is a physiological truth that is utilized daily by the intelligent physician when he orders the drinking of large amounts of water to aid the organism in ridding itself of any poison, as the toxin of an infectious disease, for example. How the secretion of water by the kidney may be made a continuous affair we have learned from our previous discussion. How it must make for a continuous secretion of dissolved substance is apparent from what follows.

Let us recall here our division of the urinary secretory system into its three parts: the blood, the secreting membrane, and the urine, and our brief characterization of the first as a liquid colloid in which various crystalloids are dissolved, the second as a solid colloid also containing various crystalloids, and the third as a watery solution of various crystalloids (practically) free from colloids. Thus far our discussion has shown that under the conditions normally existing in the body no water can be introduced into the blood without getting the secretion of an equal amount as urine. And what is secreted as urine is water and only secondarily do substances come to be dissolved in it, so that it assumes a chemical composition which permits it to be characterized as urine. Let us see now what must happen if some soluble[1] (or pseudo-soluble) substance is introduced into the blood. To simplify the problem and not make our discussion unnecessarily long, let us think of the blood as one homogeneous system, and the urinary membrane as another. Under such circumstances one of three possibilities presents itself from a physico-chemical standpoint.

[1] The word soluble is used in these paragraphs in its broadest sense, so as to include even the pseudo-soluble (colloidal) substances.

The dissolved substance may distribute itself uniformly throughout the blood and the urinary membrane, or it may be present in either a greater or a less concentration in the urinary membrane than in the blood. Just what will happen is dependent upon the nature of the dissolved substance and the physical and chemical composition of the blood and the urinary membrane at the time. Of greatest importance are such facts as the presence and absence of lipoids, the character of the colloids concerned, and the state of these colloids as determined by the presence of acids, alkalies, salts, or various non-electrolytes. In other words, the laws of partition and the laws of adsorption again come into play. These differences in the distribution of a dissolved substance between the blood and the urinary membrane are rendered strikingly apparent when dyes are used as the dissolved substances.

But this distribution of a dissolved substance between the blood and the urinary membrane represents in the end only a *static* affair, and the secretion of dissolved substances in the urine is a *dynamic* one. It requires no special comment to see now why *only through the continuous secretion of water from the kidney can a continuous separation of dissolved substance from the urinary membrane (secretion) be rendered possible. The presence of water in Bowman's capsule and in the uriniferous tubules introduces the third phase into our secretory system and breaks down continuously the equilibrium that is trying to become established between the dissolved substance in the blood and the dissolved substance in the urinary membrane.*

The attempt to establish an equilibrium between the dissolved substances in the urinary membrane and the dissolved substances in the urine (originally only water) as it passes down the uriniferous tubules makes for a diffusion of dissolved substances out of the urinary membrane, and so tends to destroy all the time that water is being secreted by the kidney, the equilibrium, which is trying to be established between the dissolved substances in the blood and the dissolved substances in the urinary membrane. When now we recall the physico-chemical fact that when any dissolved substance is offered simultaneously a liquid colloid, a solid

colloid, and water (as is the case in the kidney) an *unequal* distribution of the dissolved substance between the three phases is the *rule*, then we will have no difficulty in understanding why a difference in quantitative composition between the blood, kidney tissue, and urine, so far as dissolved substances are concerned, is also the rule. *Wherefore a "selective" secretion is to be expected rather than to be wondered at.*

Further than this we cannot pursue this subject at this time. In passing I would only like to point out that the fruits of colloid chemistry help us to understand even the most radical differences that exist between secretions and their source. None is perhaps more striking than the strongly acid reaction of the urine or the gastric juice against the practically neutral reaction of its source, the blood. But even these can be accounted for through the selective absorption by the colloids of the urinary membrane of the sodium-di-hydrogen phosphate, and by the colloids of the gastric mucosa of the hydrochloric acid of the blood. Such a concentration of an acid by colloids from very dilute solutions of acid salts or acids has been proved directly by Goppelsroeder.

Our considerations show how, corresponding with differences in the colloidal constitution of the different parts of the urinary tubule, we may find qualitative and quantitative differences in the selective secretion by them of the various constituents of the blood. That such differences in function exist physiologists have long believed. It makes no difference, of course, as to where we consider the water of the urine to be secreted. If this is in the glomeruli, as generally held (but not as yet experimentally proved), then we can imagine the water to leach out the various urinary constituents from the secreting membrane as it passes down the uriniferous tubule on its way to the pelvis of the kidney. If water is secreted by several or all portions of the uriniferous tubule, the problem remains essentially the same.

Our theory also permits of the reabsorption of water, or of dissolved substances, or of both from the fluid passing down the uriniferous tubules as postulated by some observers. It cannot of course, as yet be accepted that such a reabsorption does occur

physiologically. That a reabsorption can occur is undoubtedly correct, but the experiments made to furnish evidence for such a belief unquestionably interfere with the normal function of the kidney.

X. CONCLUDING REMARKS.

I have deemed it purposeless to review in detail all the theories that have been proposed from time to time to account for œdema. Such a task would not be easy, for the contentions of the various authors cannot always be stated in brief and do them justice. Too often this is because they have mixed their excellent experimental findings with the particular hypothesis which they were attempting to raise to the dignity of a theory; and too often also do we find good attempts to account for œdema on a mechanical basis mixed with the vague conceptions of the activities of "living" protoplasm. Any effort, therefore, to analyze the contributions of an author to the general subject of the nature and the cause of œdema must distinguish carefully between the value of that which this author may have contributed to the *experimental* side of the subject and to the *theoretical*.

Richard Bright made one of the first attempts to account for œdema when he tried to find in the loss of albumin from the body in nephritis a cause for the thinning of the blood (hydremia). Such hydremic blood, he reasoned, would then pass easily through the bloodvessels and into the tissues, and so cause the latter to swell. An experimental investigation of Bright's hypothesis forms the basis of the much-discussed work of Julius Cohnheim and Ludwig Lichtheim.[1] These authors found that the injection of enormous quantities of sodium chloride solution into the veins of various animals did not bring about an œdema similar in distribution to that observed in Bright's disease, and so decided that hydremia alone, or a hydremia connected with an increase in the amount of blood circulating in the bloodvessels (hydremic

[1] Virchow's Archiv, 1877, lxix, 106; also Cohnheim, Allgemeine Pathologie, Zweit Auflage, Berlin, 1882, i, 430.

plethora), could not be responsible for the œdema of nephritis. Cohnheim and Lichtheim could only obtain a collection of fluid in the peritoneal cavity in their infusion experiments and some œdema of the intestines and the various glands of the body. Experiments carried on by a number of authors since the work of Cohnheim and Lichtheim confirm, in the main, their findings. Some, however, discovered a distinct œdema of the skin and cutaneous tissues generally, so that the picture of the generalized anasarca of nephritis or heart disease was much more closely approximated.

In a long series of experiments on rabbits, made with an entirely different object in view, I found it necessary to inject intravenously such amounts of sodium chloride solution as were used by these authors. I found invariably that if the injections were only continued *long enough* the rabbits always developed the most intense general œdemas. The œdema is in other words more a function of the time than of the amount of fluid injected. How are these œdemas to be interpreted? Simply by noting this: *Rabbits subjected to such prolonged and great sodium chloride injections suffer from lack of oxygen.* In the later hours of the experiments this becomes so great that the animals are distinctly cyanotic. As soon as we have such a state of lack of oxygen we have the conditions at hand that increase the affinity of the tissue colloids for water, as our previously detailed experiments have shown, and so these tissues are placed in a position to absorb water from the circulating liquid in the blood and lymphvessels.

Just why in such experimentally induced œdemas the abdominal organs, for example, should develop the œdema sooner than the subcutaneous tissues is a matter that needs separate investigation. Predilection for certain regions of the body is characteristic also of various clinical forms of œdema (œdema of nephritis, œdema of heart disease). The colloids of different tissues are different, the demand for oxygen is much greater in the glandular organs than in the connective tissues, etc. Just *how* the sodium chloride injections produce the lack of oxygen will also have to be analyzed. Simple dilution of the blood, the increased work

thrown on the heart in pumping this blood, that thrown on the various glandular organs in separating the salt solution from what is the normal blood, the effect of the salt solution on the respiration, etc., all have to be considered.

It seems to me that one fact is constantly overlooked in experiments on œdema that are made on the higher animals: the necessity of furnishing an adequate supply of water to the tissues. This is not an easy matter to control in mammals, and it is for this reason that I chose to do most of my experiments with frogs, which may be dropped into water and so be allowed to absorb all the water they can take up through the skin. As mammals cannot be relied upon to drink voluntarily as much water as we might like to have them consume, one is always in the predicament of wondering just how much water ought to be injected through that stomach tube, and in experiments in which only one part of an animal is supposed to become œdematous, an inadequate water supply means too often that the affected part, in order to become œdematous, must first rob some other tissue with a lesser affinity for water before it can satisfy its own needs. After our remarks on the role of the colloids in œdema, it is, of course, self-evident that the mere consumption of water does not increase an œdema after the affinity of the tissue colloids for water has once been satisfied.[1]

There is no difficulty in understanding why Cohnheim's experiments, in which he combined the infusion of sodium chloride solution with moderate injury to a part, always led to the development of an œdema more promptly than the infusion alone. The moderate injury (heat, sunburn, iodine application) simply brought about by indirect means, the so necessary change in the colloids of the tissues, and the increased affinity for water once being established the water of the sodium chloride infusion quickly satisfied it.

The interpretation of another experimental observation of

[1] It is *possible* that mere consumption of water may increase the collections of fluid in the body cavities (ascites, hydrothorax, hydropericardium), though this question has not yet been studied. Such a conclusion seems justified on the hypothetical basis that the "secretion" into these cavities is similar to the secretion of urine.

Cohnheim[1] seems to me to need revision. Cohnheim found that an animal which has been bled repeatedly, and injected after each bleeding with a sodium chloride solution, finally develops a general œdema, and interpreted this as an œdema of cachexia, caused through an increased permeability of the bloodvessel walls, determined primarily through a hydremia. Would it not be a simpler interpretation to say that through these frequent bleedings the animal becomes anemic—that is to say, his organs get into a state of lack of oxygen—and when a supply of water is furnished the tissues, whether through a sodium chloride infusion or in any other way, they simply take this up?

We need not further discuss the inadequacy of the blood pressure theory to account for œdema. While Cohnheim regarded blood pressure as one of the two great factors concerned in the production of œdema, he also recognized that severe œdemas occur in animals when no change whatsoever in blood pressure is apparent. To account for an œdema under such circumstances he had recourse to an "increased permeability of the bloodvessel walls." If in the light of our modern physico-chemical conceptions we try to say just what is meant by this, we have to define the bloodvessel wall as a colloidal membrane. From physico-chemical observations we know that the permeability of such colloidal membranes is alterable, so this far Cohnheim is on safe ground. But of what consequence would an increased permeability of the bloodvessels be from a pathological standpoint? To force liquids through the bloodvessel walls is not to force them into the tissues. And the fluid of an œdematous tissue is very decidedly in the cells themselves. Cohnheim's hypothesis would simply squeeze the œdema fluid as far as the outer wall of the capillaries. If we try to aid Cohnheim's conception of permeability and make it extend to all protoplasm, then we are getting the cause of our œdema right where we have tried to say it is, namely, in the tissues themselves; and then our problem is simply that of how tissues hold their water. In this the forces that have been

[1] Allgemeine Pathologie, Zweite Auflage, Berlin, 1882, i, 498.

suggested as active—not only the variable affinity of colloids for water, but the previously suggested osmotic pressure, with or without Overton's conception of lipoidal surface layers—are so infinitely greater than the highest grades of blood pressure that pathologists have ever registered that the two cannot be compared.

The more recent experiments of Magnus have added much to our knowledge of the experimental side of œdema. His results, too, are usually interpreted as lending support to Cohnheim's conception of the increased permeability of bloodvessel walls as a factor in the production of œdema. How well they support the belief that the cause of œdema is to be sought in a change in the colloidal constitution of the tissues is readily evidenced by the following. Magnus found that animals which are transfused *after death* always develop a general anasarca. Living animals do not do so as readily as the dead, but they do it readily if deeply chloroformed or etherized or injected with arsenic. In place of these words we could write, *placed in a condition of lack of oxygen with an adequate supply of water*. Magnus also found that animals which have their kidneys removed develop an œdema if injected with sodium chloride solution a day or two after the operation. This is because at the end of this time the tissue colloids have either directly or indirectly been so altered by the metabolic products which should have been excreted through the kidneys that their affinity for water has been distinctly increased.

With these remarks, which have been introduced simply to illustrate how I think the experimental results of the score of workers who have busied themselves with this problem of œdema should be interpreted, we will close our discussion. It is readily apparent that through experimental analysis the part played by the blood and the lymph circulations has gradually become less prominent. From having been looked upon as alone determining the amount of water held by the tissues, we have come to find that the tissues are largely their own masters in this regard. *The blood and lymph circulations carry fluid to the tissues and away from them, but what the tissues will take up or give off rests with*

them. Only as these circulatory systems carry to the tissues substances which directly threaten their existence, or fail to remove such as the tissues have produced, which if allowed to accumulate will overcome them, only in so far are the circulatory systems masters of the tissues.

Of this possible role of the tissues pathologists have not all been ignorant, but for the most part their ideas regarding it have been vague. All the more credit, therefore, belongs to Jacques Loeb,[1] and after him to W. B. Cannon,[2] who not only first tried to prove through experiment that the problem of œdema is essentially a problem of the tissues, but suggested for its explanation a physico-chemical force (osmotic pressure) which if not adequate was at least of such a nature as could be conceived active in the living body.

What now has been accomplished by this finding that the amount of water held by the tissues is essentially an expression of their colloidal state? Its chief virtue lies in this: It places the problem. When we speak as we have done throughout this paper of the "affinity" of the colloids for water, we have not used this word unthinkingly. An affinity is not a clearly defined force, but we have chosen it to cover a present lack of knowledge concerning the nature of the forces underlying this very important relation existing between a (hydrophilic) emulsion colloid and the water it contains. Physical chemistry has not yet settled for us what this is, but toward the answer to this question it is now striving. When it is obtained we will have to strike out this mysterious word "affinity" and write into its place the names of such clearly defined forces as physical chemistry may choose to dictate.

[1] Pflüger's Archiv, 1898, lxxi, 468.

[2] American Journal of Physiology, 1902, vi, 91. Cannon showed that the cause of increased intracranial pressure after injury is dependent upon changes in the tissues of the brain itself which enable this organ to absorb an increased amount of water. He interpreted his findings as in favor of Loeb's ideas of œdema. They are more readily interpretable on the basis of our colloidal conceptions of œdema. Had Cannon's results received the recognition which their worth merits, pathologists, clinicians, and surgeons in their discussion of the source of increased intracranial pressure would not still be seeking in blood pressure the origin of a force greater than itself, for the swelling brain is able to shut off its own arterial blood supply.

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